Roman V. Rudenko, Sergey A. Komykhov,* Vladimir I. Musatov, Irina S. Konovalova, Oleg V. Shishkin, and Sergey M. Desenko

Scientific and Technological Complex "The Institute for Single Crystals," National Academy of Science of Ukraine, Kharkiv 61001, Ukraine
*E-mail: komykov@isc.kharkov.com
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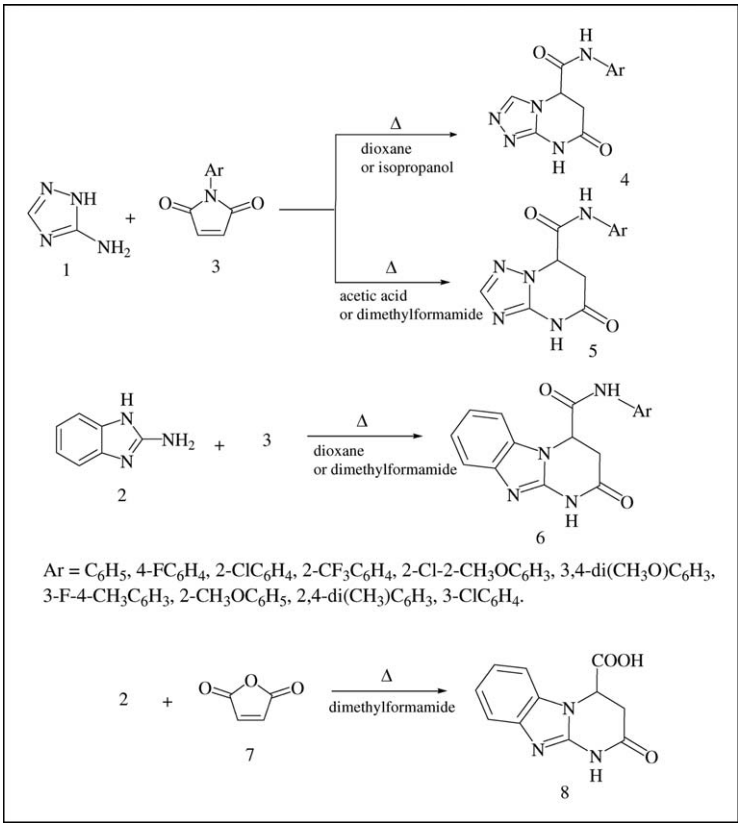

The reaction of 3-amino-1,2,4-triazole (**1**) with *N*-arylmaleimides leads to azolopyrimidines **4** and **5**. The 2-aminobenzimidazole (**2**) in the reaction with **3** gives the pyrimidobenzimidazoles **6**. In similar conditions, the reaction of amine **2** with maleic anhydride (**7**) leads to formation of 2-oxo-1,2,3,4-tetrahydropyrimido[1,2-a]benzimidazole-4-carboxylic acid (**8**). The structures of **4**, **5**, **6**, and **8** were proved by X-Ray and NOE NMR measurements.

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INTRODUCTION

The interest to reactions of *N*-aryl imides of maleic acid with different organic reagents is determined by their high synthetic potential. There are many examples of their use as dienophiles [1] in the Diels-Alder reactions, leading to different bi- or tricyclic compounds. Reactions of *N*-arylmaleimides with substituted thioureas and thiosemicarbazides leading to thiazolidone derivatives are broadly investigated [2].

Unfortunately, there are only a low number of reports concerning the behavior of *N*-arylmaleimides with 1,3-dinucleophiles; according to these reports, the direction of such reactions seems to be ambiguous (Scheme 1). For example, it was reported [3] that refluxing of substituted 6-aminouracil (**9**) or its alkylthio derivative (**10**) with maleic anhydride in acetonitril or dimethylformamide leads to formation of corresponding pyrrolo[2,3-d]pyrimidines (**11**, **12**), whereas reaction of **9** or **10** with maleimide occurs only as C-alkylation at position 5 of pyrimidine ring leading to compounds **13** and **14**, respectively. Another report [4,5] describes the reaction of 6-aminouracil (**15**) and its thio derivative (**16**) with

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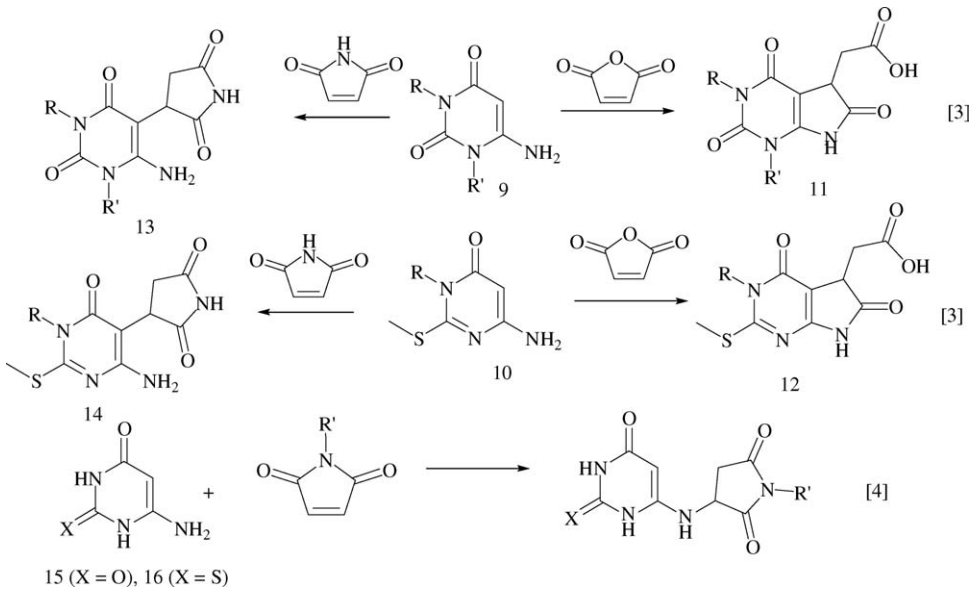
Scheme 1



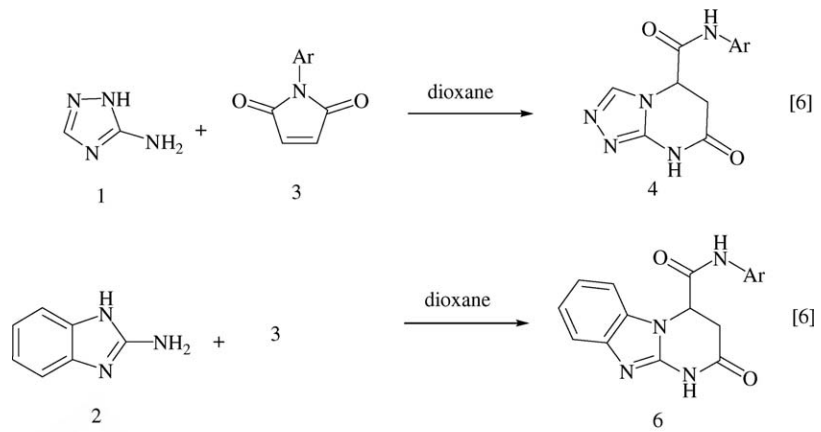
N-aryl-substituted maleimides by refluxing in isopropanol, which occurs as *N*-alkylation with participation of amino group. There is formation of more comlicated heterocyclic systems described by reactions of 6-aminouraciles and their analogs with maleic anhydride or maleimide [3].

The reaction of aminoazoles containing the amidine moiety, especially, 3-amino-1,2,4-triazole (**1**) and 2-aminobenzimidazole (**2**), with *N*-aryl derivatives of maleimides was firstly reported at [6], according to which the reaction leads to formation of azolopyrimidine derivatives **4** and **6**; the structure assignment was made based exclusively on ^{1}H-NMR spectra in this case (Scheme 2).

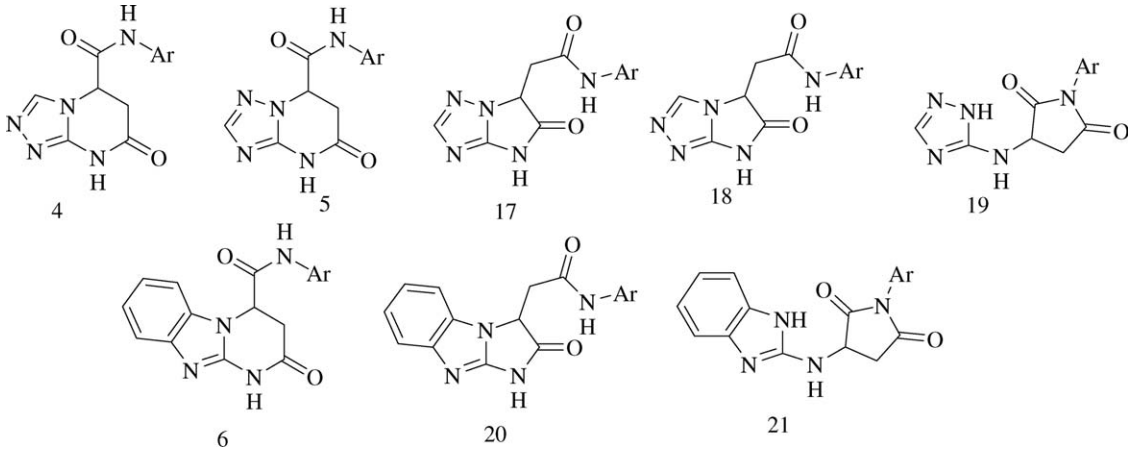
Our previous research showed that in the reactions of hererocyclic aminoazoles, like **1** and similar, with carbonyl bielectrophiles different isomeric products can be obtained. The situation becomes more complicated when bielectrophilic component of such reaction has more than two electrophilic centers (like compound **3**). As an instance, the reaction of amine **1** with 1,2-dibenzoylethylene could be mentioned [7] where three products were obtained which structure corresponded to attack of electrophile on all three endocyclic nitrogens in **3**. Taking into account, the data given in Ref. 7 and polyelectrophilic nature of compound **3**, by establishing the structure of products described in Ref. 6 additional data are necessary to be involved.

The aim of this work was the investigation of behavior of *N*-aryl maleimides in reactions with 3-amino-1,2,4-triazole and 2-aminobenzimidazole. Taking into account the described above results about the ambiguity in the direction of reactions of maleimides and maleic anhydride with

Scheme 2



Scheme 3



binucleophiles and amines **1** and **2** with bielectrophiles, the structures 4-6, 17-21 (Scheme 3) could be considered.

RESULTS AND DISCUSSION

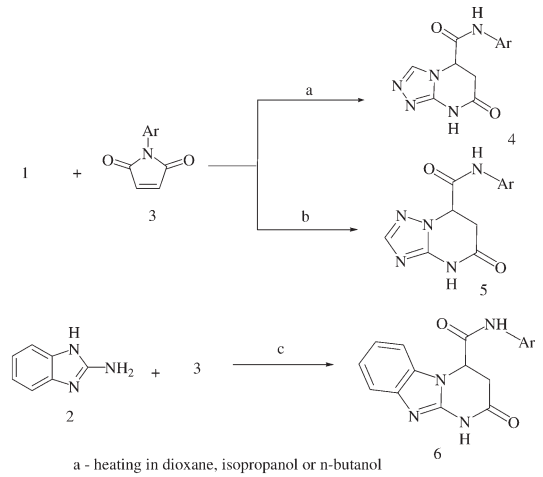
Reaction of *N*-arylmaleimides (**3**) with 3-amino-1,2,4-triazole (**1**) was carried out in different solvents: by heating in dioxane (on conditions described in Ref. 6), in ethanol and *n*-penthanol, in acetic acid and by melting together without solvent by 150–160°C. As a result, compounds **4a–g** and **5a–g** were prepared (Scheme 4). It was established that when carrying out in dioxane or isopropanol reaction leads regioselectively to formation of compounds **4**. Compounds 5 can be obtained selectively by heating of **3** and **1** in acetic acid during not more than 1 h; carrying out this reaction on this conditions for a longer time led to mixtures of compounds 4 and 5. The same result was obtained by using of toluene or dimethylformamide as a solvent. In all cases, according to ^{1}H-NMR data, the individual compounds were isolated.

The structure of **4a–g** and **5a–g** was assigned based on ^{1}H-NMR including NOE experiments, NMR ^{13}C, mass-spectrometry. The ^{1}H-NMR spectra of **4a**–**g** and **5a**–**g** were very similar and contained signals of ABX system, protons of aromatic rings, secondary amino groups, and triazole proton. It was noticed that the chemical shift values in the ^{1}H-NMR spectra of products obtained by heating in acetic acid (compounds **5**) were different from corresponding values for the products obtained in alcohols or dioxane (**4**), especially, the chemical shift values for triazole protons. For instance, compounds **4** had a signal for triazole proton at 7.74–7.76 ppm, whereas compounds 5 the corresponding signal was situated at 8.30–8.35 ppm. The difference in δ values for protons of ABX system in **4** and **5** was not more than 0.1 ppm. It is necessary to notice that analytical data and ^{1}H-NMR data for compound **4a**, which was prepared similar to described in Ref. 6, were absolutely consistent with described values. Compounds **4** showed enhancement of the signal of triazole proton (at 8.33 ppm) by irradiation of the H_X proton of ABX system (the signal at 5.30 ppm) in the NOE experiment (Scheme 5); compound **5** showed no such effect, which is consistent with structures of **4** and **5** given above.

In addition, structures of **4c** and **5d** were confirmed by its X-ray analysis (Fig. 1).

The tetrahydropyrimidine ring of the compound **5d** adopts asymmetric half-chair conformation (the puckering parameters [8] are $S = 0.48$, $\Theta = 43.4°$, $\Psi = 21.3°$). Deviations of the C(4) and C(5) atoms from the mean plane of the remaining atoms of the ring are −0.30 Å and 0.18 Å, respectively. The carbamide fragment of the substituent at C(5) atom is visibly noncoplanar to the C(4)—C(5) endocyclic bond (the C(4)—C(5)—C(6)—O(2) torsion angle is −65.9(3)°) due to repulsion between hydrogen atoms (shortened intramolecular contact H(5)...H(5NA) 2.13 Å as compared with van der Waals radii sum [9] 2.34 Å). The aryl group adopts the *ap*-conformation relatively the C(5)—C(6) bond (the C(5)—C(6)—N(5)—C(7) torsion angle is −172.2(2)°) and it is turned with respect to the C(6)—N(5) bond (the C(6—N(5)—C(7)—C(8) torsion angle is −58.0(3). Such orientation of this substituent leads to the appearance of the H(5NA)...F(3) shortened intramolecular contact 2.52 Å (2.56 Å), which cannot be considered as hydrogen bond owing to very small value of the N—H...F angle (108°). In the crystal phase molecules of **5d** form centrosymmetric dimers due to the N(4)—H(4NA)...N(3)′ ($-x$, $-y+1$, $-z+1$) intermolecular hydrogen bond (H...N 2.07 Å N—H...N 166°).

Scheme 4



a - heating in dioxane, isopropanol or n-butanol
b - melting in acetic acid or dimethylformamide
c - heating in dioxane or dimethylformamide

Compound	R	Solvent	Reaction Time	Yield (%)
4a	C_6H_5-	dioxane	3 h	40
4a	C_6H_5-	isopropanol	3 h	54
4b	4-F-C_6H_4-	dioxane	3 h	36
4b	4-F-C_6H_4-	isopropanol	3 h	54
4c	2-Cl-C_6H_4-	isopropanol	3 h	51
4d	2-CF_3-C_6H_4-	n-propanol	3 h	45
4d	2- CF_3-C_6H_4-	dioxane	3 h	35
4e	5-Cl-2-CH_3O-C_6H_3-	dioxane	3 h	38
4f	3,4-di-CH_3O-C_6H_3-	isopropanol	3 h	52
4g	3-F-4-CH_3-C_6H_3-	n-propanol	3h	55
5a	C_6H_5-	acetic acid	1 h	30
5a	C_6H_5-	dimethylformamide	0.5 h	36
5b	2-CH_3O-C_6H_4-	without solvent (150-160ºC)	5 min	40
5c	2-Cl-C_6H_4-	acetic acid	1 h	27
5d	2-CF_3-C_6H_4-	acetic acid	1 h	25
5e	5-Cl-2-CH_3O-C_6H_3-	acetic acid	1 h	27
5f	2,4-di-CH_3-C_6H_3-	without solvent (150-160ºC)	5 min	42
5g	3-Cl-C_6H_4-	dimethylformamide	0.5 h	32

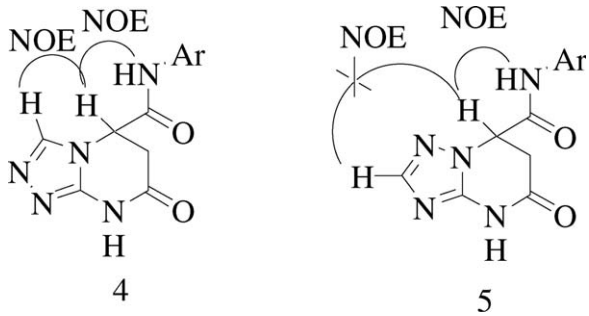
These dimers form the infinite chains along [0 1 0] crystallographic direction due to the N(5)—H(5NA)...O(2)′ (x, $y-1$, z) intermolecular hydrogen bond (H...O′ 2.12 Å, N—H...O′ 170°).

The compound **4c** is observed in the crystal phase with water solvent molecules with the 1:1 ratio. Two molecules (A and B) with some differences in geometrical parameters are observed in the asymmetric part of the unit cell. The tetrahydropyrimidine ring in both isomers adopts almost identical half-chair conformation (the puckering parameters [8] are $S = 0.62$, $\Theta = 40.6°$, $\Psi = 24.7°$ in A, $S = 0.61$, $\Theta = 42.2°$, $\Psi = 24.3°$ B). Deviations of the C(4) and C(5) atoms from the mean plane of the remaining atoms of the ring are −0.26 Å and 0.36 Å, respectively in both A and B molecules. The carbamide fragment of the substituent at the C(5) atom is almost coplanar to the N(3)—C(5) endocyclic bond (the N(3)—C(5)—C(6)—O(2) torsion angle is 8.1(5)° A, 8.3(5)° B). The o-chlorophenyl group is practically coplanar to the carbamide fragment (the N(3)—C(5)—C(6)—O(2) torsion angle is 6.4(7)° A, 5.6(7) B). Such position of this group is stabilized by the C(12)—H(12)...O2 intramolecular hydrogen bond (H...O 2.13 Å C-H...O 126° in molecule A, H...O 2.15 Å C-H...O 126° in B). The o-chlorophenyl substituent is disordered over two position due to the rotation around the C(7)—N(5) bond with populations 60:40% in molecules A and B. In the crystal phase, molecules **4c** form dimers between molecules A and B due to the N(4)—H(4NA)...N(2B)′ (x, $y-1$, z) intermolecular hydrogen bond (H...N 2.02 Å, N—H...N 164°). In the crystal form hydrophilic cavity which contain water molecules (Fig. 2).

We also studied the reaction of 2-aminobenzimidazole (**2**) with *N*-arylmaleimides (**3**) by heating in dimethylformamide or dioxane (Scheme 6). The single product (**6**) was isolated; its analytical data were consistent with given in [6]. According to NMR data including NOE experiments (Scheme 6), the structure of **6** was assigned as given on Scheme 4. The ^{1}H-NMR spectra of **6** contained except signals of ABX system and aryl rings, additionally signals for ABDC system of benzimidazole ring. The enhancement of one of the signals of benzimidazole moiety (7.43 ppm) by irradiation of H_X proton (signal at 5.38 ppm) in the NOE experiment (Scheme 6) allowed to propose the structure of **6** as shown on Scheme 6.

Finally, we investigated the reaction of amine **2** with maleic anhydride (7). Heating of components in dimethylformamide during 5 led to formation of 2-oxo-1,2,3,4-tetrahydropyrimido[1,2-a]benzimidazole-4-carbox-

Scheme 5



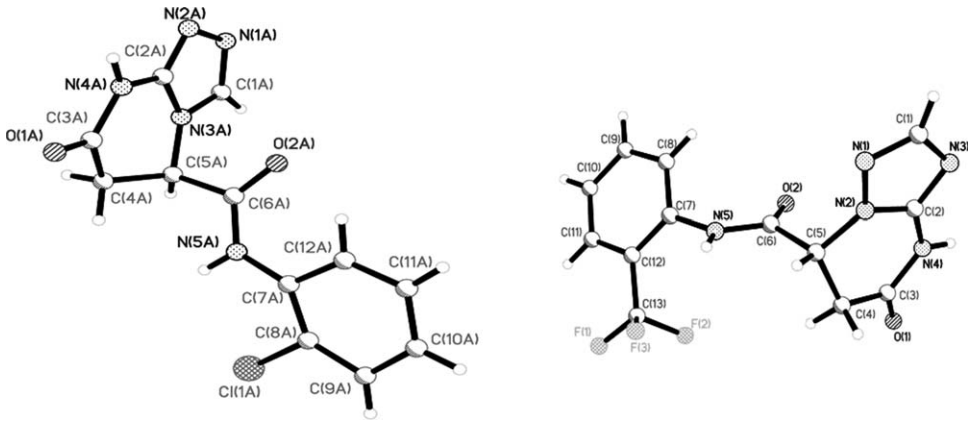


Figure 1. Molecular structures of compounds **4c** and **5d**, respectively with numerations of nonhydrogen atoms used in the structural analysis.

ylic acid (**8**), Scheme 7. The structure assignment was achieved by use of the same approach as for compound **6**: the irradiation of the methine proton (signal at 5.46 ppm) in the NOE experiment showed the enhancement of the signal at 7.38 ppm (of the benzimidazole proton).

EXPERIMENTAL

General. Melting points were determined with a Kofler apparatus. The yields of 3a–e are given after their crystallization. The ^{1}H- and ^{13}C-NMR spectra were recorded in DMSO-d_6 at 200 MHz (50 MHz for ^{13}C) on a Varian Mercury VX-200 spectrometer, internal standard was $Si(CH_3)_4$. The EI mass spectra were obtained on Varian 1200L with electron energy 70 eV.

X-ray diffraction study. The crystals of **5d** ($C_{13}H_{10}F_3N_5O_2$) are monoclinic. At 293 K, a = 20.517(1), b = 4.884(1), c = 14.135(1) Å, β = 97.02(1), V = 1406 (1) Å^3, M_r = 325.26, Z = 4, space group $P2_1/c$, d_{calc} = 1.537 g/cm^3, μ(MoKα= 0.135 mm^{-1}, F(000) = 664. Intensities of 7738 reflections (2421 independent, R_{int} =0.037) were measured on the «Xcalibur-3» diffractometer (graphite monochromated MoKα radiation, CCD detector, ω-scaning, $2\Theta_{max} = 50°$).

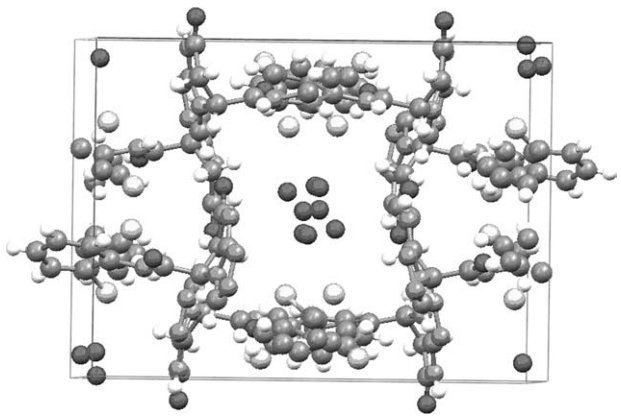
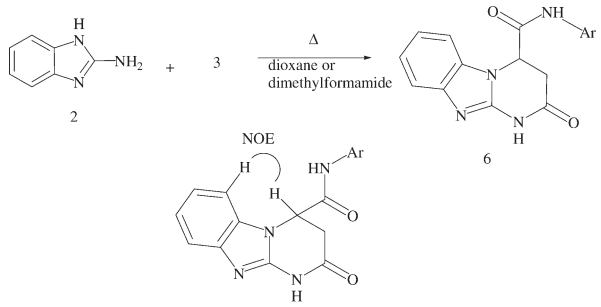


Figure 2. Cavity in the crystal of **4c** containing water.

The crystals of **4c** ($C_{12}H_{10}N_5O_2Cl_1 \cdot H_2O$) are monoclinic. At 293 K, a = 13.385(1), b = 13.268(1), c = 18.043(1) Å, β = 90.13(4), V = 3204.2(3)Å^3, M_r = 615.40, Z = 8w, space group $P2_1/n$, d_{calc} = 1.276 g/cm^3, μ (MoKα) = 0.254 mm^{-1}, F(000) = 1264. Intensities of 19076 reflections (5534 independent, R_{int} =0.061) were measured on the «Xcalibur-3» diffractometer (graphite monochromated MoKα radiation, CCD detector, ω-scaning, $2\Theta_{max} = 50°$).

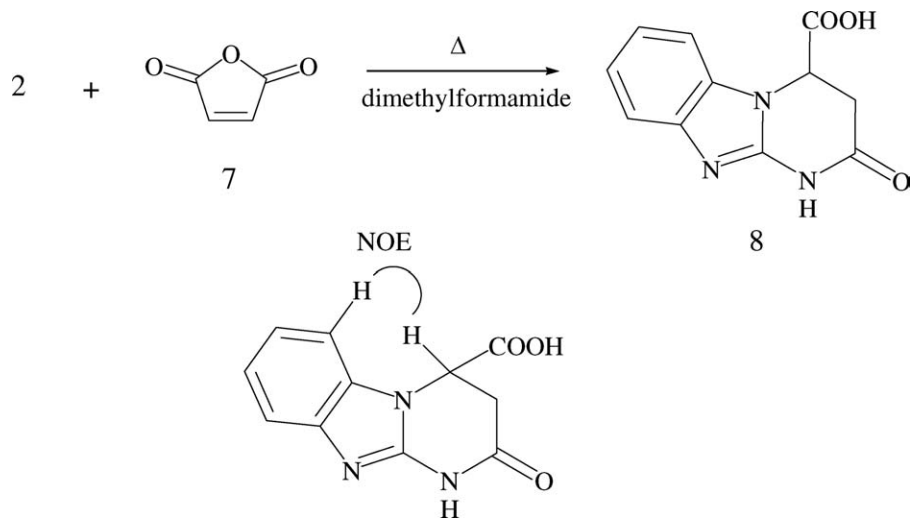
The structures were solved by direct method using SHELX97 package [10]. The restrains for the bond lengths (C_{Ar}—C_{Ar} 1.38 Å, Csp^3-Cl 1.79 Å) in the disordered fragments were applied during refinement of the structure **4c**. Positions of the hydrogen atoms were located from electron density difference maps and refined by ''riding'' model with $U_{iso} = nU_{eq}$ of the carrier atom (n = 1.5 for methyl group and n = 1.2 for

Scheme 6



Compound	Ar	Solvent	Reaction time	Yield, %
6a	C_6H_5	dimethylformamide	5 min	60
6a	C_6H_5	dioxane	2 h	40
6b	4-$CH_3OC_6H_4$	dimethylformamide	5 min	64
6b	4-$CH_3OC_6H_4$	dioxane	2 h	45
6c	2-ClC_6H_4	dimethylformamide	5 min	77
6d	2-$CF_3C_6H_4$	dimethylformamide	5 min	75
6e	4-ClC_6H_4	dimethylformamide	5 min	70
6f	2,4-di-$CH_3C_6H_4$	dimethylformamide	5 min	62
6g	4-$COOHC_6H_4$	dimethylformamide	5 min	72

Scheme 7



other hydrogen atoms. Positions of the hydrogen atoms on the water molecules could not be detected.

Full-matrix least-squares refinement of the structures against F^2 in anisotropic approximation for nonhydrogen atoms using 7738 (**5d**), 19076 (**4c**) reflections were converged to: $wR_2 = 0.142$ ($R_1 = 0.049$ for 1390 reflections with $F > 4\sigma(F)$, $S = 0.882$) for structure **5d** and $wR_2 = 0.264$ ($R_1 = 0.093$ for 2200 reflections with $F > 4\sigma(F)$, $S = 0.785$) for structure **4c**. The final atomic coordinates and crystallographic data for molecules **5d** and **4c** have been deposited to with the Cambridge Crystallographic Data Centre, UK, and are available on request quoting the deposition numbers CCDC 773608 for **4c** and CCDC 773609 for **5d**).

General procedure for the synthesis of 7-oxo-N-aryl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine-5-carboxamide 4a–g. A mixture of the 3-amino-1,2,4-triazole (**1**, 0.42 g, 0.005 mol) and corresponding *N*-arylmaleimide (**3**, 0.005 mol) in 10 mL of appropriate solvent was refluxed for 3 h. After cooling, the precipitate formed was filtered off and recrystallized from acetone and air-dried.

7-Oxo-N-phenyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine-5-carboxamide (4a). Colorless crystals, m.p. > 300°C. ^{1}H-NMR (DMSO-d_6): δ 2.81 (1H, dd, $^3J_{AX}$ =2.9, $^2J_{AB}$ = 16.7 Hz, H_A), 3.33 (1H, dd, $^3J_{BX}$ =7.5 Hz, 16.7 Hz, H_B), 5.30 (1H, dd, H_X), 7.12–7.04 (1H, m, *p*-ArH), 7.36–7.27 (2H, m, *m*-ArH), 7.57–7.52 (2H, m, *o*-ArH), 8.33 (1H, s, 2-H), 10.52 (1H, s, NHCOAr), 11.5 (1H, br. s, 8-H, NH). ^{13}C-NMR (DMSO-d_6): δ 33.5, 52.3, 119.5, 123.9, 128.6, 128.6, 137.9, 139.4, 149.3, 165.8, 166.0. Anal. Calcd. for $C_{12}H_{11}N_5O_2$: C, 56.03; H, 4.31; N, 27.22%. Found: C, 55.1; H, 4.2; N, 26.8.

7-Oxo-N-(4-fluorophenyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine-5-carboxamide (4b). Colorless crystals, m.p. > 300°C. ^{1}H-NMR (DMSO-d_6): δ 2.84 (1H, dd, $^3J_{AX}$ = 3.1 Hz, $^2J_{AB}$ =16.8 Hz, H_A), 3.34 (1H, dd, $^3J_{BX}$ = 7.3 Hz, H_B), 5.29 (1H, dd, H_X), 7.22–7.13 (2H, m, *m*-ArH), 7.62–7.54 (2H, m, *o*-ArH), 8.34 (1H, s, 2-H), 10.57 (1H, s, NHCOAr), 11.5 (1H, br s, 8-H, NH). ^{13}C-NMR (DMSO-d_6): δ 33.7, 52.4, 115.45 (d, $^2J(^{13}C^{19}F)$ = 22.7 Hz, *m*-C_{Ar}), 121.3 (d, $^3J(^{13}C^{19}F)$ = 8.0 Hz, *o*-C_{Ar}), 134.5 (d, $^4J(^{13}C^{19}F)$ = 2.2 Hz, C_{Ar}), 139.8, 149.5, 158.4 (d, $^1J(^{13}C^{19}F)$ = 241 Hz, *p*-C_{Ar}), 166.1, 166.2. *m/z* (EI, rel. %): 191 (2), 137 (19), 135 (16), 121 (23), 84 (100).

7-Oxo-N-(2-chlorophenyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine-5-carboxamide (4c). Colorless crystals, m.p. > 300°C. ^{1}H-NMR (DMSO-d_6) δ 2.83 (1H, dd, $^3J_{AX}$ = 3.0, $^2J_{AB}$ = 16.8 Hz, H_A), 3.33 (1H, dd, $^3J_{BX}$ = 7.4 Hz, H_B), 5.44 (1H, dd, H_X), 7.37–7.18 (2H, m, ArH), 7.62–7.48 (2H, m, ArH), 8.33 (1H, s, 2-H), 10.18 (1H, s, NHCOAr), 11.5 (1H, br s, 8-H_{NH}).

7-Oxo-N-(2-(trifluoromethyl)phenyl)-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyrimidine-5-carboxamide (4d). Colorless crystals, m.p. < 300°C. ^{1}H-NMR (DMSO-d_6): δ 2.81 (1H, dd, $^3J_{AX}$ = 3.1, $^2J_{AB}$ = 16.8 Hz, 6-H_A), 3.33 (1H, dd, $^3J_{BX}$ = 7.5 Hz, 6-H_B), 5.42 (1H, dd 5-H_X), 7.54–7.45 (2H, m, ArH), 7.78–7.67 (2H, m, ArH), 8.31 (1H, s, 2-H), 11.80–10.0 (2H, br s, NHCOAr + 8-H_{NH}). ^{13}C-NMR (DMSO-d_6): δ 33.4, 51.7, 125.9 (1C, q, $^1J(^{13}C^{19}F)$ = 271 Hz, CF_3), 125.0 (1C, q, $^2J(^{13}C^{19}F)$ = 30.3 Hz, C_{Ar}-CF_3), 126.3, (1C, q, $^3J(^{13}C^{19}F)$ = 4.8 Hz, *m*-C_{Ar}), 127.3, 129.9, 132.9, 134.0, (C_{Ar}), 139.4, 149.2, 165.6, 167.4.

7-Oxo-N-(5-chloro-2-methoxyphenyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine-5-carboxamide (4e). Colorless crystals, m.p. > 300°C. ^{1}H-NMR (DMSO-d_6): δ 2.77 (1H, dd, $^3J_{AX}$ = 2.8 Hz, $^2J_{AB}$ = 16.9 Hz, 6-H_A), 3.30 (1H, dd, $^3J_{BX}$ = 7.5 Hz, 6-H_B), 3.87 (3H, s, CH_3O), 5.50 (1H, dd, 5-H_X), 7.22–7.06 (2H, m, ArH), 7.98–7.93 (1H, m, *o*-ArH), 8.32 (1H, s, 2-H), 10.0 (1H, br s, NHCOAr), 11.3 (1H, br s, 8-H_{NH}); *m/z* (EI, rel. %): 321 (2) [M^+], 157 (10), 155 (20), 140 (36), 138 (34), 137 (29), 127 (13), 84 (100).

7-Oxo-N-(3,4-dimethoxyphenyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine-5-carboxamide (4f). Colorless crystals, m.p. > 300°C. ^{1}H-NMR (DMSO-d_6): δ 2.81 (1H, dd, $^3J_{AX}$ = 2.7, $^2J_{AB}$ = 16.8 Hz, 6-H_A), 3.32 (1H, dd, $^3J_{BX}$ = 7.5 Hz, 6-H_B), 3.71 (6H, s, 2*CH_3O), 5.26 (1H, dd, 5-H_X), 6.91 (1H, m, *m*-ArH), 7.05 (1H, m, *o*-ArH), 7.28 (1H, m, *o′*-ArH) 8.33 (1H, s, 2-H), 10.36 (1H, br s, NHCOAr), 11.4 (1H, br s, 8-H_{NH}).

7-Oxo-N-(3-fluoro-4-methylphenyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine-5-carboxamide (4g). Colorless crystals, m.p. 296–297°C. ^{1}H-NMR (DMSO-d_6): δ 2.18 (3H, s, CH_3), 2.81 (1H, dd, $^2J_{AX}$ = 2.9 Hz, $^3J_{AB}$ = 16.8 Hz, 6-H_A), 3.33 (1H, dd, $^3J_{BX}$ = 7.6 Hz, 6-H_B), 5.28 (1H, dd, 5-H_X), 7.29–7.15 (2H, m, ArH), 7.50–7.43 (1H, m, ArH), 8.32 (1H, s,

2-H), 10.62 (1H, br s, NHCOAr), 11.5 (1H, br s, 8-H_{NH}); *m/z* (EI, rel. %): 289 (5) [M^+], 137 (6), 124 (13), 84 (100).

General procedure for the synthesis of 5-oxo-N-aryl-4,5,6,7-tetrahydro-[1,2,4]triazolo[1,5-a]pyrimidine-7-carboxamide 5a–g. A mixture of the 3-amino-1,2,4-triazole (**1**, 0.42 g, 0.005 mol) and of the corresponding *N*-arylmaleimide (**3**, 0.005 mol) in 1 mL of appropriate solvent was refluxed for 1 h. After cooling, mixture was diluted of acetone. The precipitate formed was filtred off and air-dried.

5-Oxo-N-phenyl-4,5,6,7-tetrahydro-[1,2,4]triazolo[1,5-a]pyrimidine-7-carboxamide (5a). Colorless crystals, m.p. > 300°C. ^{1}H-NMR (DMSO-d_6): δ 2.88 (1H, dd, $^3J_{AX}$ = 2.0 Hz, $^2J_{AB}$ = 16.8 Hz, 6-H_A), 3.51 (1H, dd, $^3J_{BX}$ = 8.2 Hz, 6-H_B), 5.25 (1H, dd, 7-H_X), 7.14–7.07 (1H, m, *p*-ArH), 7.37–7.29 (2H, m, *m*-ArH), 7.59–7.55 (2H, m, *o*-ArH), 7.77 (1H, s, 2-H), 10.52 (1H, s, NHCOAr), 11.5 (1H, br s, 4-H_{NH}). Anal. Calcd. for $C_{12}H_{11}N_5O_2$: C, 56.03; H, 4.31; N, 27.22%. Found: C, 54.5; H, 4.3; N, 26.6.

5-Oxo-N-(2-chlorophenyl)-4,5,6,7-tetrahydro-[1,2,4]triazolo[1,5-a]pyrimidine-7-carboxamide (5b). Colorless crystals, m.p. > 300°C. ^{1}H-NMR (DMSO-d_6) δ_H 2.87 (1H, dd, $^3J_{AX}$ = 1.8 Hz, $^2J_{AB}$ = 16.8 Hz, 6-H_A), 3.55 (1H, dd, $^3J_{BX}$ = 8.5 Hz, 6-H_B), 5.48 (1H, dd, 7-H_X), 7.38–7.20 (2H, m, ArH), 7.67–7.50 (2H, m, ArH), 7.79 (1H, s, 2-H), 10.20 (1H, br s, NHCOAr), 11.50 (1H, br s, 4-H_{NH}). Anal. Calcd. for $C_{12}H_{10}ClN_5O_2$: C, 49.41; H, 3.46; N, 24.01%. Found: C, 48.9; H, 3.4; N, 24.2.

5-Oxo-N-(2-(trifluoromethyl)phenyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a] pyrimidine-7-carboxamide (5c). Colorless crystals, m.p. > 300°C. ^{1}H-NMR (DMSO-d_6): δ 2.78 (1H, dd, $^3J_{AX}$ = 1.8 Hz, $^2J_{AB}$ = 16.8 Hz, 6-H_A), 3.57 (1H, dd, $^3J_{BX}$ = 8.2 Hz, 6-H_B), 5.39 (1H, dd, 7-H_X), 7.54–7.44 (2H, m, ArH), 7.77–7.66 (2H, m, ArH), 7.78 (1H, s, 2-H), 10.26 (1H, br s, NHCOAr), 11.50 (1H, br s, 4-H_{NH}). ^{13}C-NMR (DMSO-d_6): δ 33.5, 54.6, 123.1 (1C, q, $^1J(^{13}C^{19}F)$ = 274 Hz, CF_3), 124.6 (1C, q, $^2J(^{13}C^{19}F)$ = 29.8 Hz, C_{Ar}-CF_3), 126.1, (1C, q, $^3J(^{13}C^{19}F)$ = 5.1 Hz, *m*-C_{Ar}), 127.0, 129.3, 132.7, 133.8, (1C, q, $^4J(^{13}C^{19}F)$ = 2.0 Hz, C_{Ar}), 150.1, 150.6, 165.7, 167.3.

5-Oxo-N-(5-chloro-2-methoxyphenyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a] pyrimidine-7-carboxamide (5d). Colorless crystals, m.p. > 300°C. ^{1}H-NMR (DMSO-d_6): δ 2.83 (1H, dd, $^3J_{AX}$ = 1.8, $^2J_{AB}$ = 17.1 Hz, 6-H_A), 3.49 (1H, dd, $^3J_{BX}$ = 8.4 Hz, 6-H_B), 3.87 (3H, s, CH_3O), 5.60 (1H, dd, 7-H_X), 7.20–7.07 (2H, m, ArH), 7.78 (1H, s, 2-H), 8.00 (1H, m, *o*-ArH), 10.0 (1H, br s, NHCOAr), 11.5 (1H, br s, 4-H_{NH}). ^{13}C-NMR (DMSO-d_6): δ 33.6, 54.8, 56.1, 112.8, 120.8, 123.8, 124.2, 127.5, 148.4, 150.3, 150.7, 166.0, 166.9; *m/z* (EI, rel. %): 323 (9) [M^+], 321 (27) [M^+], 138 (98), 137 (100), 110 (47), 109 (36), 84 (48).

5-Oxo-N-(2,4-dimethylphenyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine-7-carboxamide (5e). Colorless crystals, m.p. > 300°C. ^{1}H-NMR (DMSO-d_6): δ 2.13 (3H, s, CH_3), 2.24 (3H, s, CH_3), 2.85 (1H, dd, $^3J_{AX}$ = 2.2 Hz, $^2J_{AB}$ = 16.9 Hz, 6-H_A), 3.52 (1H, dd, $^3J_{BX}$ = 8.1 Hz, 6-H_B), 5.33 (1H, dd, 7-H_X), 7.06–6.92 (2H, m, ArH), 7.22–7.18 (1H, m, ArH), 7.78 (1H, s, 2-H), 9.87 (1H, br s, NHCOAr), 11.3 (1H, br s, 4-H_{NH}). ^{13}C-NMR (DMSO-d_6): δ 17.7, 20.5, 34.1, 55.1, 124.9, 125.4, 130.9, 131.9, 132.5, 135.1, 150.3, 150.9 166.64, 166.65.; *m/z* (EI, rel. %): 285 (8) [M^+], 138 (68), 137 (100), 84 (39), 83 (85).

5-Oxo-N-(3-chlorophenyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine-7-carboxamide (5f). Colorless crystals, m.p. > 300°C. ^{1}H-NMR (DMSO-d_6) δ_H 2.84 (1H, dd, $^3J_{AX}$ = 1.8 Hz, $^2J_{AB}$ = 16.9 Hz, 6-H_A), 3.52 (1H, dd, $^3J_{BX}$ = 8.1 Hz, 6-H_B), 5.31 (1H, dd, 7-H_X), 7.07–6.94 (2H, m, ArH), 7.20–7.18 (2H, m, ArH), 7.77 (1H, s, 2-H), 10.53 (1H, br s, NHCOAr), 11.3 (1H, br s, 4-H_{NH}); *m/z* (EI, rel. %): 293 (33), 291 (100) [M^+], 138 (68), 137 (100), 84 (37), 83 (85). Anal. Calcd. for $C_{12}H_{10}ClN_5O_2$: C, 49.41; H, 3.46; N, 24.01%. Found: C, 49.2; H, 3.5; N, 24.1.

General procedure for the synthesis of 2-oxo-N-aryl-1,2,3,4-tetrahydropyrimido[1,2-a]benzimidazole-4-carboxamide 6a–g. A mixture of the 2-aminobenzimidazole (**2**, 0.4 g, 0.003 mol) and of the corresponding *N*-arylmaleimide (**3**, 0.003 mol) in 1 mL of DMF was refluxed for 10 min. After cooling, mixture was diluted of acetone, the precipitate formed was filtred off and air dried.

2-Oxo-N-phenyl-1,2,3,4-tetrahydropyrimido[1,2-a]benzimidazole-4-carboxamide (6a). Coloress crystals, m.p. > 300°C. ^{1}H-NMR (DMSO-d_6): δ 2.92 (1H, d, $^2J_{AB}$ = 16.7 Hz, 3-H_A), 3.50 (1H, dd, $^3J_{BX}$ = 7.8 Hz, 3-H_B), 5.38 (1H, d, 4-H_X), 7.18–7.03 (3H, m, ArH), 7.37–7.26 (2H, m, ArH), 7.49–7.39 (2H, m, ArH), 7.61–7.51 (2H, m, ArH), 10.63 (1H, s, NHCOAr), 11.5 (1H, br s, 1-H_{NH}). ^{13}C-NMR (DMSO-d_6): δ 33.4, 51.9, 108.3, 117.0, 119.5, 120.5, 121.4, 123.8, 128.4, 132.3, 137.7, 141.7, 148.3, 166.0, 166.8. Anal. Calcd. for $C_{17}H_{14}N_4O_2$: C, 66.66; H, 4.61; N, 18.29%. Found: C, 66.6; H, 4.5; N, 18.1.

2-Oxo-N-(4-methoxyphenyl)-1,2,3,4-tetrahydropyrimido[1,2-a]benzimidazole-4-carboxamide (6b). Coloress crystals, m.p. > 300°C. ^{1}H-NMR (DMSO-d_6): δ 2.89 (1H, d, $^2J_{AB}$ = 16.8 Hz, 3-H_A), 3.47 (1H, dd, $^3J_{BX}$ = 7.8 Hz, 3-H_B), 3.72 (3H, s, CH_3O), 5.34 (1H, d 4-H_X), 6.92–6.84 (2H, m, ArH), 7.17–7.08 (2H, m, ArH), 7.51–7.37 (4H, m, ArH), 10.36 (1H, s, NHCOAr), 11.4 (1H, br s, 1-H_{NH}); Anal. Calcd. for $C_{18}H_{16}N_4O_3$: C, 64.28; H, 4.79; N, 16.66%. Found: C, 63.8; H, 4.8; N, 16.4.

2-Oxo-N-(2-chlorophenyl)-1,2,3,4-tetrahydropyrimido[1,2-a]benzimidazole-4-carboxamide (6c). Coloress crystals, m.p. > 300°C. ^{1}H-NMR (DMSO-d_6): δ 2.92 (1H, d, $^2J_{AB}$ = 16.9 Hz, 3-H_A), 3.52 (1H, dd, $^3J_{BX}$ = 8.1 Hz, 3-H_B), 5.60 (1H, d, 4-H_X), 7.37–7.08 (4H, m, ArH), 7.64–7.40 (4H, m, ArH), 10.25 (1H, s, NHCOAr), 11.4 (1H, br s, 1-H_{NH}); *m/z* (EI, rel. %): 342 (39) [M^+], 340 (13) [M^+], 186 (11), 158 (7), 144 (28), 133 (39), 131 (12), 127 (15), 126 (16), 90 (100). Anal. Calcd. for $C_{17}H_{13}ClN_4O_2$: C, 59.92; H, 3.85; N, 16.44%. Found: C, 59.5; H, 3.84; N, 16.4

2-Oxo-N-(2-(trifluoromethyl)phenyl)-1,2,3,4-tetrahydropyrimido[1,2-a]benzimida-zole-4-carboxamide (6d). Coloress crystals, m.p. > 300°C. ^{1}H-NMR (DMSO-d_6): δ 2.87 (1H, d, $^2J_{AB}$ = 16.7 Hz, 3-H_A), 3.56 (1H, dd, $^3J_{BX}$ = 7.9 Hz, 3-H_B), 5.53 (1H, d, 4-H_X), 7.22–7.08 (2H, m, ArH), 7.54–7.35 (4H, m, ArH), 7.79–7.61 (2H, m, ArH), 10.36 (1H, s, NHCOAr), 11.5 (1H, br s, 1-H_{NH}); Anal. Calcd. for $C_{18}H_{13}F_3N_4O_2$: C, 57.76; H, 3.5; N, 14.97%. Found: C, 57.6; H, 3.6; N, 14.9.

2-Oxo-N-(4-chlorophenyl)-1,2,3,4-tetrahydropyrimido[1,2-a]benzimidazole-4-carboxamide (6e). Coloress crystals, m.p. > 300°C. ^{1}H-NMR (DMSO-d_6): δ 2.91 (1H, d, $^2J_{AB}$ = 16.8 Hz, 3-H_A), 3.49 (1H, dd, $^3J_{BX}$ = 7.8 Hz, 3-H_B), 5.35 (1H, d, 4-H_X), 7.14–7.05 (2H, m, ArH), 7.45–7.31 (4H, m, ArH), 7.61–7.52 (2H, m, ArH), 10.74 (1H, s, NHCOAr), 11.4 (1H, br s, 1-H_{NH}). ^{13}C-NMR (DMSO-d_6): δ 33.3, 51.9, 108.3, 117.1, 120.6, 121.0, 121.4, 127.6, 128.4, 132.3, 136.6, 141.7, 148.3, 166.1, 167.0; *m/z* (EI, rel. %): 342 (24) [M^+], 340 (8) [M^+],

186 (39), 158 (14), 144 (59), 133 (84), 131 (21), 127 (28), 126 (27), 90 (100). Anal. Calcd. for $C_{17}H_{13}ClN_4O_2$: C, 59.92; H, 3.85; N, 16.44%. Found: C, 59.3; H, 3.8; N, 16.3.

2-Oxo-N-(2,4-dimethylphenyl)-1,2,3,4-tetrahydropyrimido[1,2-a]benzimidazole-4-carboxamide (6f). Coloress crystals, m.p. > 300°C. ^{1}H-NMR (DMSO-d_6): δ 2.07 (3H, s, CH_3), 2.22 (3H, s, CH_3), 2.91 (1H, d, $^2J_{AB}$ = 17.2 Hz, 3-H_A), 3.52 (1H, dd, $^3J_{BX}$ = 8.2 Hz, 3-H_B), 5.47 (1H, d, 4-H_X), 7.22–6.9 (5H, m, ArH), 7.54–7.37 (2H, m, ArH), 9.93 (1H, s, NHCOAr), 11.5 (1H, br s, 1-H_{NH}); *m*/*z* (EI, rel. %): 334 (74) [$\overline{M}^+$], 186 (41), 159 (44), 158 (53), 144 (93), 133 (100), 131 (27), 121 (63), 117 (45), 90 (70). Anal. Calcd. for $C_{19}H_{18}N_4O_2$: C, 68.24; H, 5.43; N, 17.76%. Found: C, 68.1; H, 5.4; N, 17.6.

2-Oxo-N-(4-carboxy)-1,2,3,4-tetrahydropyrimido[1,2-a]benzimidazole-4-carboxamide (6g). Coloress crystals, m.p. > 300°C. ^{1}H-NMR (DMSO-d_6): δ 2.95 (1H, d, $^2J_{AB}$ = 17.0 Hz, 3-H_A), 3.51 (1H, dd, $^3J_{BX}$ = 8.1 Hz, 3-H_B), 5.41 (1H, d, 4-H_X), 7.15–7.07 (2H, m, ArH), 7.46–7.38 (2H, m, ArH), 7.68–7.63 (2H, m, ArH), 7.90–7.85 (2H, m, ArH), 10.92 (1H, s, NHCOAr), 12.0 (2H, br s, 1-H_{NH}+COOH). Anal. Calcd. for $C_{18}H_{18}N_4O_4$: C, 61.71; H, 4.03; N, 15.99%. Found: C, 60.9; H, 4.1; N, 15.7.

2-Oxo-1,2,3,4-tetrahydropyrimido[1,2-a]benzimidazole-4-carboxylic acid (6h). A mixture of the 2-aminobenzimidazole (**2**, 0.4 g, 0.003 mol) and of the maleic anhydride (**3**, 0.3 g, 0.003 mol) in 1 mL of DMF was refluxed for 5 min. After cooling, mixture was diluted of acetone, the precipitate formed was filtred off and air dried.

Coloress crystals, m.p. > 300°C. ^{1}H-NMR (DMSO-d_6): δ 2.90 (1H, d, $^2J_{AB}$ = 16.8 Hz, 3-H_A), 3.42 (1H, dd, $^3J_{BX}$ = 7.8 Hz, 3-H_B), 5.49 (1H, d, 4-H_X), 7.16–7.04 (2H, m, ArH), 7.44–7.35 (2H, m, ArH), 11.8 (2H, br s, 1-H_{NH}+COOH). ^{13}C-NMR (DMSO-d_6): δ 32.9, 50.3, 108.9, 117.0, 120.7, 121.4, 132.7, 141.6, 147.6, 166.2, 170.0. Anal. Calcd. for $C_{11}H_9N_3O_3$: C, 57.14; H, 3.92; N, 18.17%. Found: C, 57.5; H, 4.2; N, 17.9.

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