Unusual direction of three-component reactions involving 2-amino-4-arylimidazoles and carbonyl compounds leading to Knoevenagel-Michael adducts

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DOI: http://dx.doi.org/10.3998/ark.5550190.0014.306

Abstract
Three-component reaction of 2-amino-4-arylimidazoles, aldehydes and dimedone or barbituric acid proceeds in an unusual direction and instead of imidazo[1,2-*a*]pyrimidine derivatives gives Knoevenagel-Michael adducts having abnormally low reactivity in heterocyclizations.

Keywords: Multicomponent reaction, heterocycles, Michael addition, microwave-assisted synthesis, utrasound-assisted synthesis

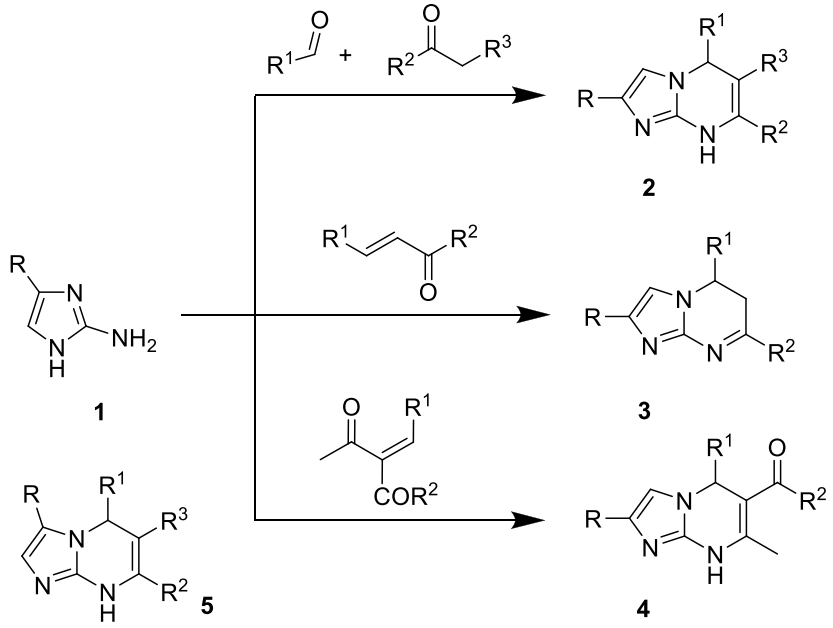
Introduction

2-Amino-1*H*-imidazole containing molecules are of particular interest, especially within the realm of medicinal chemistry. For example, several classes of marine natural products possessing this fragment were recently discovered and identified.[1] Many of compounds based on aminoimidazole moiety display a broad range of biological properties and were recognized as H_1- and H_2-receptor agonists and antagonists,[2] 5-HT_3 receptor antagonists,[3] antibacterial remedies and other.[4] Recently, it was demonstrated that compounds of this type occurring in nature inhibit and disperse bacterial biofilms through a non-bactericidal mechanism.[5]

In the past few years multicomponent reactions (MCRs) of broad range of 2-aminoazoles with CH-acids and aromatic aldehydes have attracted the interest of the synthetic community since the formation of different condensation products can be expected depending on the specific conditions and structure of the starting materials.[6] Multicomponent reactions often use simple

and readily available starting materials that makes them an excellent synthetic tool for combinatorial chemistry, creating high scaffold diversity and a large variety in functional groups.

To the best of our knowledge the behavior of 2-amino-1*H*-imidazoles in multicomponent reactions has been studied insufficiently and there are relatively few publications dealing with heterocyclizations of their 4-substituted derivatives.[7,8] There is only one publication by Ryabukhin *et al.* which described application of 4(5)-substituted 2-aminoimidazoles **1** in multicomponent Biginelli-type reactions with aldehydes and CH-acids in the presence of TMSCl as promoter (Scheme 1).[7]



Scheme 1. Synthesis of known dihydroimidazo[1,2-*a*]pyrimidines.

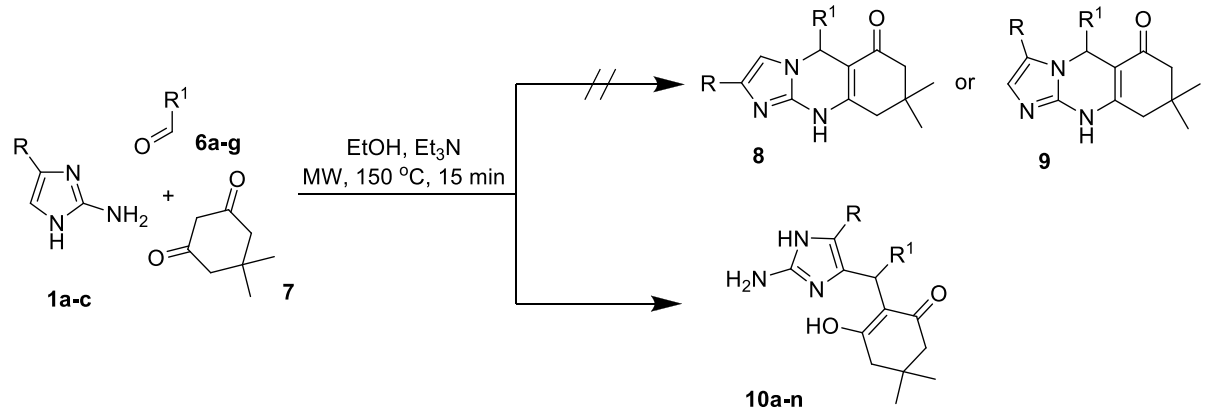
Other publication reported sequential reactions *via* preliminary synthesis of α,β-unsaturated compounds. For example, it was described synthesis of 5,6-dihydroimidazo[1,2-*a*]pyrimidines **3** by reaction of aminoimidazoles **1** with chalcones.[8a] Meng and co-authors published syntheses of dihydroimidazo[1,2-*a*]pyrimidine-6-carboxylates and -6-carboxamides **4** *via* condensation of amines **1** with enones.[8b-d] In all the cases reported only one endocyclic nucleophilic center of aminoazole was involved in the reaction and formation of compounds like 5 as well as other types was not observed.

In continuation of our recent interests in multicomponent reactions for the synthesis of small heterocyclic molecules,[6b,9] herein we report a three-component reaction of 4-aryl-2-amino-1*H*-imidazoles with aromatic aldehydes and dimedone and 1,3-dimethylbarbituric acid.

Results and Discussion

Due to the presence of several exo- and endocyclic nucleophilic reaction centers in the aminoimidazole building blocks the formation of different heterocycles, e.g. compounds **8** and **9**, may be expected in this MCR. However, it was established an unusual direction of three-component treatment of equimolar mixture of 2-aminoimidazoles **1a-c**, aldehydes **6a-g** and dimedone **7** in boiling ethanol leading to the Knoevenagel-Michael adduct **10** (Scheme 2) while fused heterocyclic compounds were not found even in trace amounts (TLC and NMR control).

In order to study an influence of reaction parameters on the condensation proceeding, the reaction of amine **1a**, dimedone **7**, and aldehyde **6a** was selected as a model one. Firstly, different protonic (EtOH, 2-PrOH, HOAc, H_2O) and aprotic (DMF, toluene) solvents and several types of additives (Et_3N, HCl, Ac_2O, p-TSA) were screened. The reactions were carried out by refluxing the starting materials in appropriate solvent for 30 min. In all the cases studied reaction proceeded exclusively with formation of adduct **10a**. The best solvents were found ethanol and DMF which allowed in the presence of Et_3N to reach 60-65% of yields. Addition of acid catalysts decreased the overall outcome of **10a** to 30-40%. Variation of the reaction time up to 72h did not change type of the final product but also considerably reduced its yields.



1a-c: a R = 4-MeC_6H_4; b R = 4-$MeOC_6H_4$; c R = 4-BrC_6H_4
6a-g: a R^1 = 4-MeC_6H_4; b R^1 = 4-$MeOC_6H_4$; c R^1 = 4-ClC_6H_4; d R^1 = 4-BrC_6H_4; e R^1 = C_6H_5; f R^1 = 4-$COOMeC_6H_4$; g R^1 = 3,4-$(MeO)_2C_6H_3$

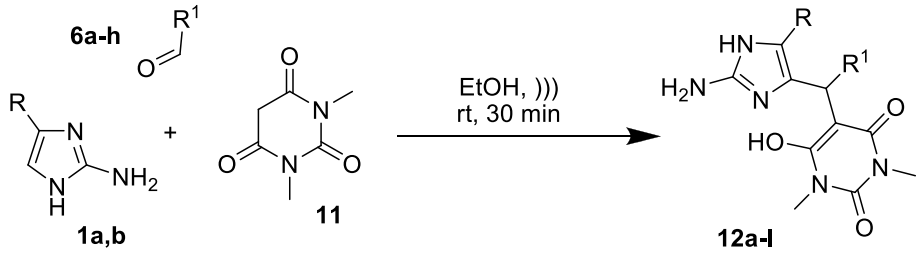
Scheme 2. Multicomponent microwave-assisted synthesis of adducts **10a-n**.

Microwave irradiation is often used for increasing efficiency of chemical processes and for tuning selectivity of organic synthesis.[10] This method was also applied for the MCRs studied. However, the treatment of the starting materials **1**, **6** and **7** which was carried out in EtOH or DMF in microwave reactor in a wide range of temperatures (120 – 190 °C) led to increasing the yields of adducts **10** (up to 82%) while formation of heterocyclic compounds **8** or **9** was not observed as well.

Based on these empirical observations a thorough optimization of the reaction conditions ultimately led to a microwave-assisted procedure which allowed isolation of adducts **10a-n** in 70-84% yields (Table 1) with purity of 97% (TLC and NMR control). The optimal synthetic conditions consist in dissolving equimolar amounts of the starting materials in ethanol containing 1.0 equivalent of Et_3N and further MW heating the reaction mixture in a sealed vial at 150 °C for 15 min.

The optimized microwave procedure were applied to closely related treatment involving 1,3-dimethylbarbituric acid **11** as one of the building blocks (Scheme 3). However, it was found that under these conditions the MCR followed with intense degradation of the reaction mixture. The same situation was observed in the case of using conventional heating in ethanol or DMF.

To solve this problem we used ultrasound-assisted synthesis which application was earlier described for increasing efficiency of organic reactions at room temperature.[11] In our case ultrasonication of the mixture containing 2-aminoimidazole **1a,b**, barbituric acid **11** and aromatic aldehydes **6a-h** in ethanol at room temperature for 30-45 min gave adducts **12a-l** in 68-85% yields. A presence in the reaction mixture of acidic (AcOH, HCl) or basic (Et_3N) catalysts decreased yields and purity of the compounds **12**.



1a,b: a R = 4-MeC_6H_4; b R = 4-$MeOC_6H_4$
6a-h: a R^1 = 4-MeC_6H_4; b R^1 = 4-$MeOC_6H_4$; c R^1 = 4-ClC_6H_4; d R^1 = 4-BrC_6H_4; e R^1 = C_6H_5; f R^1 = 4-$COOMeC_6H_4$; h R^1 = 4-$NO_2C_6H_4$

Scheme 3. MCR of 2-amino-4-arylimidazoles, aldehydes and 1,3-dimethylbarbituric acid.

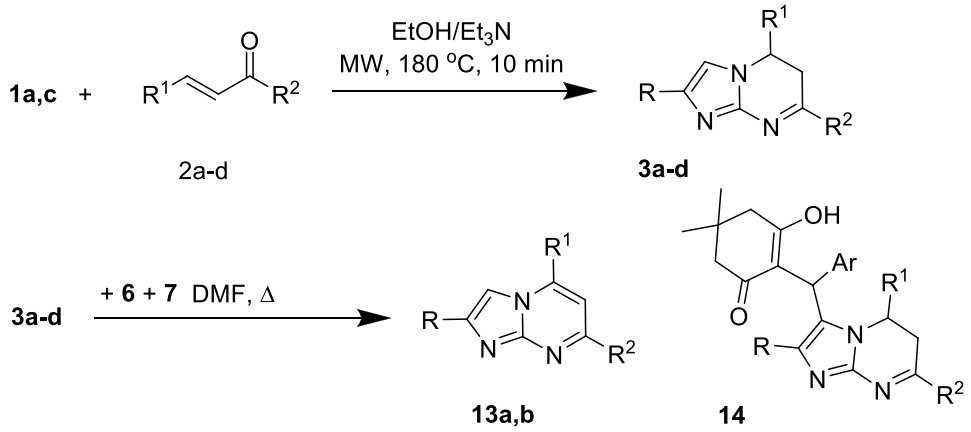
Thus, variation of the reaction conditions (solvent/additive system, temperature, time, activation type) has no influence on the unusual direction of MCRs between 2-aminoimidazoles **1**, aldehydes **6** and cyclic active methylene compounds **7** or **11**.

Numerous attempts to carry out further heterocyclization of compounds **10** and **12** into pyrrolo[1,2-*e*]imidazoles by refluxing in DFM even with help of water-consuming agents or to carry out reaction with aldehydes which should give imidazo[1,5-*a*]pyridines were unsuccessful and led to isolation of the unchanged adducts **10** or to decomposition of adducts **12**.

It was also found another unusual result: adducts **10** and **12** were not able to react with α,β-unsaturated ketones **2** with formation of imidazo[1,2-*a*]pyrimidines **14** as it had been described[8a] for starting 2-aminoimidazoles **1** (Scheme 1). Such low reactivity can be explained by the steric influence of both R-substituent and arylmethylcyclanone moiety which prevents proceeding

addition of endocyclic NH-group to enone system of ketone. Existing zwitterionic tautomeric forms (see below) may also contribute to the unusual behavior.

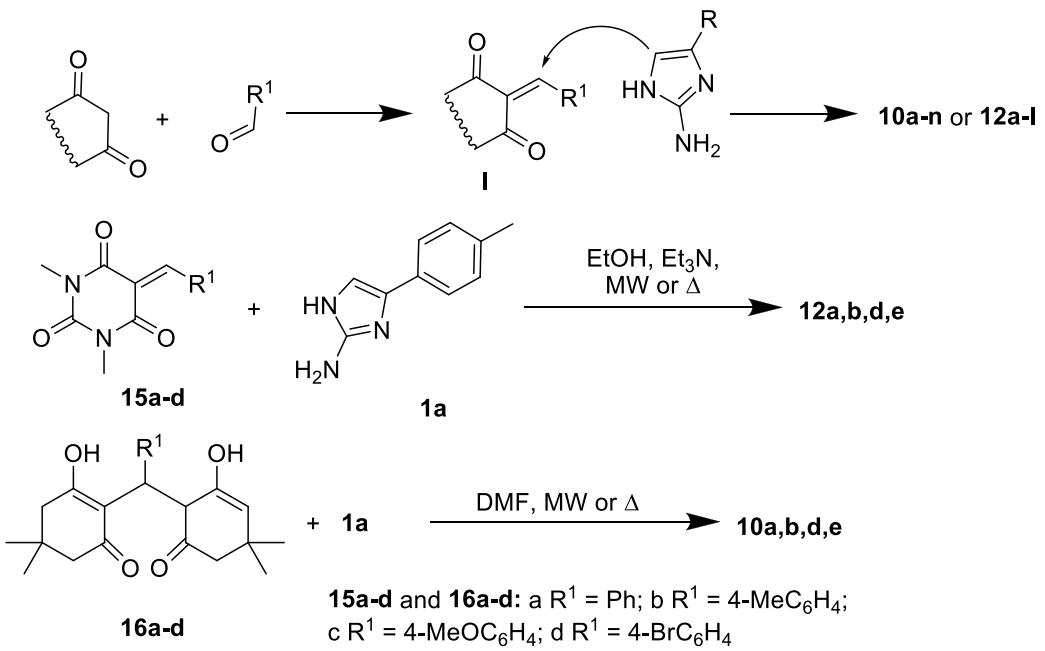
In order to synthesize heterocycles **14** the alternative sequential pathway was studied. At the first stage by microwave-assisted reaction of amines **1a,c** and chalcones **2a-d** (EtOH/Et_3N, 180 °C, 10 min) the earlier undescribed imidazo[1,2-*a*]pyrimidines **3a-d** were synthesized in 80-88% yields (Scheme 4, Table 1). However, further MCR of compounds **3** with aldehydes **6a-h** and dimedone **7** in DMF under conventional or microwave heating (120 – 190 °C) resulted in formation of heterocycles **13a,b** (73-84% yields) whereas adducts **14** were not detected.



1a,c: a R = 4-MeC_6H_4; b R = 4-BrC_6H_4
2a-d: a R^1 = 4-FC_6H_4, R^2 = 4-MeC_6H_4; b R^1 = 4-ClC_6H_4, R^2 = 4-MeC_6H_4; c R^1 = 4-$MeOC_6H_4$, R^2 = 4-MeC_6H_4; d R^1 = Ph, R^2 = 4-MeC_6H_4

Scheme 4. Synthesis of imidazo[1,2-*a*]pyrimidines.

It seems that multicomponent reactions between of 2-amino-4-arylimidazoles, aromatic aldehydes and dimedone or 1,3-dimethylbarbituric acid proceed via preliminary formation of cyclic α,β-unsaturated carbonyls **I** which enone system then is attacked by CH-nucleophilic center of azole ring (Scheme 5).



Scheme 5. Two-step procedure for the synthesis of adducts **10** and **12** from 2-aminoimidazole and α,β-unsaturated carbonyls.

Table 1. Synthesis of compounds **3**, **10**, **12** and **13**

Compound	R	R^1	R^2	Yield%
3a	4-MeC_6H_4	4-FC_6H_4	4-MeC_6H_4	88
3b	4-BrC_6H_4	4-ClC_6H_4	4-MeC_6H_4	80
3c	4-BrC_6H_4	4-$MeOC_6H_4$	4-MeC_6H_4	84
3d	4-BrC_6H_4	C_6H_5	4-MeC_6H_4	82
10a	4-MeC_6H_4	4-MeC_6H_4	-	73[a]
10b	4-MeC_6H_4	4-$MeOC_6H_4$	-	70[a]
10c	4-MeC_6H_4	4-ClC_6H_4	-	72[a]
10d	4-MeC_6H_4	4-BrC_6H_4	-	84[a]
10e	4-MeC_6H_4	C_6H_5	-	72[a]
10f	4-MeC_6H_4	4-$COOMeC_6H_4$	-	84[a]
10g	4-MeC_6H_4	3,4-$(MeO)_2C_6H_3$	-	82[a]
10h	4-$MeOC_6H_4$	4-MeC_6H_4	-	76[a]
10i	4-$MeOC_6H_4$	4-$MeOC_6H_4$	-	74[a]
10J	4-$MeOC_6H_4$	4-ClC_6H_4	-	78[a]
10k	4-$MeOC_6H_4$	4-BrC_6H_4	-	82[a]
10l	4-$MeOC_6H_4$	C_6H_5	-	71[a]
10m	4-$MeOC_6H_4$	4-$COOMeC_6H_4$	-	79[a]
10n	4-BrC_6H_4	4-MeC_6H_4	-	80[a]
12a	4-MeC_6H_4	4-MeC_6H_4	-	80

Table 1. Continued

Compound	R	R^1	R^2	Yield%
12b	4-MeC_6H_4	4-$MeOC_6H_4$	-	82
12c	4-MeC_6H_4	4-ClC_6H_4	-	71
12d	4-MeC_6H_4	4-BrC_6H_4	-	85
12e	4-MeC_6H_4	C_6H_5	-	71
12f	4-MeC_6H_4	4-$COOMeC_6H_4$	-	79
12g	4-$MeOC_6H_4$	4-MeC_6H_4	-	79
12h	4-$MeOC_6H_4$	4-$MeOC_6H_4$	-	83
12i	4-$MeOC_6H_4$	4-ClC_6H_4	-	78
12J	4-$MeOC_6H_4$	4-BrC_6H_4	-	79
12k	4-$MeOC_6H_4$	C_6H_5	-	68
12l	4-$MeOC_6H_4$	4-$NO_2C_6H_4$	-	73
13a	4-MeC_6H_4	4-FC_6H_4	4-MeC_6H_4	74
13b	4-BrC_6H_4	C_6H_5	4-MeC_6H_4	83

[a] microwave-assisted procedure

Treatment of arylidenbarbituric acids **15a-d** and aminoimidazole **1a** leading to adducts **12a,b,d,e** both under conventional and microwave (150 °C) heating confirmed this hypothesis.

Due to low synthetic availability of arylidencyclohexan-1,3-diones in addition we carried out reaction of aminoimidazole **1a** with compounds **16a-d** which also led to formation of adducts **10a,b,d,e**.

The difference between behavior of chalcones[8a] or aryliden derivatives of acetoacetic acid esters[8b-d] and cyclic α,β-unsaturated ketones **15a-d** in their reaction with aminoimidazoles **1** may be connected both with steric factors and with unfavorable for the cyclocondensation S-*cis*-configuration of the enone fragment in the compounds like **I** (Scheme 5) complicated by the high rigidity of the skeleton.

The structures of adducts **10** and **12** were established with help of elemental analyses, MS and NMR spectroscopic data and X-ray study. For instance, ^{1}H NMR spectra of compounds **10** exhibit the following signals: multiplets for the aromatic rings (6.5-8.0 ppm) and appropriate signals for their terminal substituents, a singlet for the CH proton (5.8 ppm), four doublets for the two CH_2 groups, singlet for two methyl groups (0.9 ppm), singlet for the NH_2 group (6.4-6.5 ppm) and a broad singlets for the NH- and OH-groups (or NH and NH^+ due to existing zwitterionic tautomeric forms, see below) at 11.0 and 16.0 ppm, respectively. Spectra of compounds **12** contain similar sets of signals taking into account the replacement of dimedone fragment with barbituric one.

Finally, the structure of compounds synthesized was proved by X-ray diffraction data obtained for crystal of **10d** (Figure 1).

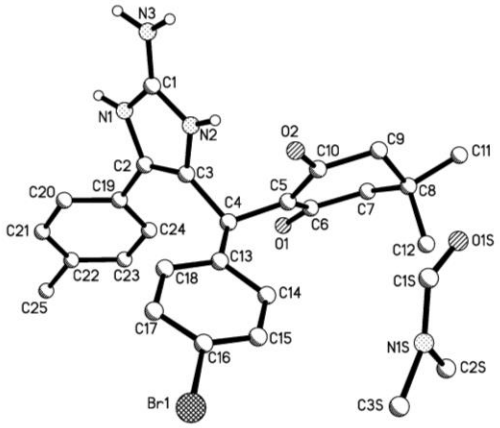


Figure 1. Structure of compound **10d** (X-ray diffraction data).

It was found that the compound **10d** exists in the crystal phase as zwitterionic tautomer with hydrogen atom located at the N1 atom of the imidazole ring. The analysis of the bond lengths demonstrates that two molecules (A and B) observed in the asymmetric part of the unit cell have the same localization of the positive charge on the N1 atom (the N1-C1 bond length (1.321(3) Å in molecule A and 1.312(4) Å in B) is close to the mean value[12] for Csp^2=N(3) bond 1.316 Å) and different localization of the negative charge (Figure 2). In the molecule A the bond lengths in the O1-C6-C5-C10-O2 fragment are alternated (O1-C6 1.261(3) Å, C6-C5 1.404(4) Å, C5-C10 1.367(4) Å, C10-O2 1.306(4) Å) that allows to assume existence of one carbonyl group in enol form with negatively charged O2 atom. In contrary in the molecule B the corresponding bond lengths of this fragment are equalized (O1-C6 1.274(4) Å, C6-C5 1.400(4) Å, C5-C10 1.414(5) Å, C10-O2 1.267(4) Å) that indicates the delocalization of the negative charge throughout all fragment.

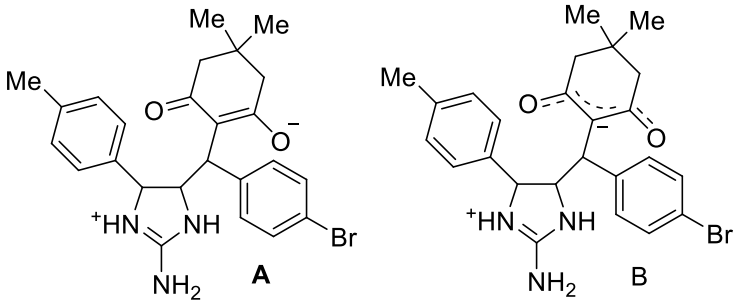


Figure 2. Zwitterionic tautomeric forms of the compound **10d** in the crystal phase according X-ray diffraction data.

Conclusions

In summary, the multicomponent reactions of 2-amino-4-arylimidazoles, aromatic aldehydes and dimedone or 1,3-dimethylbarbituric acid under conventional heating, microwave or ultrasonic

irradiation were studied and unusual directions resulting in formation of Knoevenagel-Michael adducts instead of imidazoquinazolinone fragment was established and discussed. Abnormally low reactivity of these adducts was found therefore attempts to carry out their further modifications were unsuccessful.

Experimental Section

General. Melting points were obtained on a standard melting point apparatus in open capillary tubes. ^{1}H and ^{13}C NMR were recorded on a Varian-Mercury VX-200 spectrometer (200 MHz, 50 MHz for ^{13}C) in DMSO-d_6. Mass spectra were recorded on GS/MS spectrometer Varian 1200L (70 eV) using direct input of sample. Elemental analysis was made on a EuroVector EA-3000. TLC analyses were performed on pre-coated (silica gel 60 HF_{254}) plates.
Ultrasonication was carried out with help of standard ultrasonic bath producing irradiation at 44.2 kHz in round-bottom flasks equipped with a condenser.
Microwave experiments were performed using the Emrys^{TM} Creator EXP reactor from Biotage AB possessing a single-mode microwave cavity producing controlled irradiation at 2.45 GHz. Experiments were carried out in sealed microwave process vials using high absorbance level settings and IR temperature monitoring. Reaction time reflect irradiation times at the set reaction temperature (fixed hold times).
All solvents and chemicals were obtained from standard commercial vendors and were used without any further purification.

X-ray diffraction analysis of compound 10d. C_3H_7NO are triclinic. At 293 K a = 10.439(2), b = 13.997(2), c = 20.769(3) Å, α = 75.29(1)°, β = 78.48(1)°, γ = 71.75(1)°, V = 2763.5(7) Å^3, M_r = 553.49, Z = 4, space group $P\bar{1}$, d_{calc}= 1.330 g/cm^3, μ(MoK_α) = 1.522 mm^{-1}, F(000) = 1152. Intensities of 27690 reflections (16080 independent, R_{int}=0.154) were measured on the «Xcalibur-3» diffractometer (graphite monochromated MoK_α radiation, CCD detector, ω-scaning, $2\Theta_{max}$ = 60°). The structure was solved by direct method using SHELXTL package.[13] The absorption correction was performed by multi-scan method (T_{min} =0.751, T_{max} =0.928). Positions of the hydrogen atoms were located from electron density difference maps and refined by "riding" model with U_{iso} = nU_{eq} (n= 1.5 for methyl groups and n=1.2 for other hydrogen atoms) of the carrier atom. Full-matrix least-squares refinement against F^2 in anisotropic approximation for non-hydrogen atoms using 15870 reflections was converged to wR_2 = 0.181 (R_1 = 0.079 for 3731 reflections with F>4σ(F), S = 0.768). The final atomic coordinates, and crystallographic data for molecule **10d** have been deposited to with the Cambridge Crystallographic Data Centre, 12 Union Road, CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk) and are available on request quoting the deposition numbers CCDC 881950).

General procedure for the synthesis 2,5,7-Triaryl-5,6-dihydroimidazo[1,2-*a*]pyrimidines 3a-d

Equimolar mixture (1 mmol) of 2-amino-4-arylimidazole **1a,b**, chalcone **2a-d** and Et_3N in 2 mL of ethanol was contained in sealed microwave vial and heated in the microwave reactor at 180 °C for 10 min with vigorous magnetic stirring. After cooling to ambient temperature the precipitate formed was removed by filtration, washed with $EtOH/H_2O$ (1:1) and dried at room temperature to produce the desirable compounds **3a-d**.

5-(4-Fluorophenyl)-2,7-di-*p*-tolyl-5,6-dihydro-imidazo[1,2-*a*]pyrimidine (3a). Yellow powder of mp 240-242 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 2.28 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 3.34-3.38 (m, 1H. 6-CH), 3.46-3.50 (m, 1H, 6-CH), 5.63-5.67 (m, 1H, 5-CH), 7.32 (s, 1H. 3-CH), 7.10-7.30 (m, 8H, ArH), 7.65 (d, 2H, *J* 8.0 Hz, ArH), 7.94 (d, 2H, *J* 8.2 Hz, ArH) ppm; MS (EI, 70 eV): *m/z* 396 (29) [M^+], 395 (100), 320 (50), 301 (11), 300 (50), 273 (24%). Anal. Calcd for $C_{26}H_{22}FN_3$: C, 78.96; H, 5.61; N, 10.63. Found: C, 78.86; H, 5.49; N, 10.49.

2-(4-Bromophenyl)-5-(4-chlorophenyl)-7-*p*-tolyl-5,6-dihydroimidazo[1,2-*a*]pyrimidine (3b). Yellow crystals of mp 239-241 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 2.33 (s, 3H, CH_3), 3.36-3.40 (m, 1H, 6-CH), 3.50-3.54 (m, 1H, 6-CH), 5.63-5.67 (m, 1H, 5-CH), 7.21 (d, 2H, *J* 8.5 Hz, ArH), 7.27 (d, 2H, *J* 8.1 Hz, ArH), 7.48 (s, 1H, 3-CH), 7.40-7.54 (m, 4H, ArH), 7.73 (d, 2H, *J* 8.4 Hz, ArH), 7.94 (d, 2H, *J* 8.5 Hz, ArH) ppm; MS (EI, 70 eV): *m/z* 477 (29) [M^+], 475 (73), 320 (50), 296 (13), 284 (36), 193 (14%). Anal. Calcd for $C_{25}H_{19}BrClN_3$: C, 62.98; H, 4.02; N, 8.81. Found: C, 62.87; H, 3.90; N, 8.68.

2-(4-Bromophenyl)-5-(4-methoxyphenyl)-7-*p*-tolyl-5,6-dihydroimidazo[1,2-*a*]pyrimidine (3c). Yellow powder of mp 230-232 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 2.27 (s, 3H, CH_3), 3.35-3.39 (m, 1H, 6-CH), 3.48-3.52 (m, 1H, 6-CH), 3.80 (s, 3H, OCH_3), 5.60-5.64 (m, 1H, 5-CH), 7.02 (d, 2H, *J* 8.9 Hz, ArH), 7.09-7.18 (m, 4H, ArH), 7.33 (s, 1H, 3-CH), 7.57 (d, 2H, *J* 8.4 Hz, ArH), 7.66 (d, 2H, *J* 8.1 Hz, ArH), 8.01 (d, 2H, *J* 8.9 Hz, ArH) ppm; MS (EI, 70 eV): *m/z* 473 (19) [M^+], 472 (63), 471 (31), 363 (14), 316 (45), 291 (21), 182 (16%). Anal. Calcd for $C_{26}H_{22}BrN_3O$: C, 66.11; H, 4.69; N, 8.90. Found: C, 66.01; H, 4.54; N, 8.75.

2-(4-Bromophenyl)-5-phenyl-7-*p*-tolyl-5,6-dihydroimidazo[1,2-*a*]pyrimidine (3d). Yellow powder of mp 248-250 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 2.27 (s, 3H, CH_3), 3.35-3.39 (m, 1H, 6-CH), 3.48-3.52 (m, 1H, 6-CH), 5.63-5.67 (m, 1H, 5-CH), 7.10-7.19 (m, 4H, ArH), 7.30-7.38 (m, 3H, ArH), 7,37 (s, 1H, 3-CH), 7.63-7.71 (m, 4H, ArH), 7.98 (d, 2H, *J* 8.6 Hz, ArH) ppm; MS (EI, 70 eV): *m/z* 443 (100) [M^+], 442 (67), 441 (99), 440 (34), 367 (14), 365 (34), 364 (67), 363 (22), 339 (45), 338 (24), 337 (45), 336 (15), 155 (17), 130 (21), 129 (15), 128 (13), 116 (13), 115 (14%). Anal. Calcd for $C_{25}H_{20}BrN_3$: C, 67.88; H, 4.56; N, 9.50. Found: C, 67.79; H, 4.44; N, 9.38.

General procedure for the synthesis of 2-((2-Amino-1*H*-imidazol-4-yl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-enones (10a-n)

Equimolar mixture (1 mmol) of 2-amino-4-arylimidazole **1a-c**, dimedone **7**, the appropriate aromatic aldehyde **6a-g** and Et_3N in 2 mL of ethanol was placed in microwave vial (5 mL) and

capped. The mixture was microwave irradiated at 150°C for 15 min with vigorous magnetic stirring. After cooling to room temperature 3 mL of EtOH/H_2O mixture (1:1) was added and the crude reaction mixture was stirred for 10 min. The precipitate formed was collected by filtration, washed with EtOH/H_2O (1:1), and dried at room temperature to produce the adduct **10a-n**.

2-((2-Amino-5-(*p*-tolyl)-1*H*-imidazol-4-yl)(*p*-tolyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone (10a). White powder of mp 195-196 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 0.94 (s, 6H, CH_3), 2.06-2.13 (m, 4H, CH_2), 2.18 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 5.89 (s, 1H, CH), 6.42 (br s, 2H, NH_2), 6.89 (d, 2H, *J* 8.6 Hz, ArH), 6.95 (d, 2H, *J* 8.6 Hz, ArH), 7.15 (d, 2H, *J* 8.4 Hz, ArH), 7.28 (d, 2H, *J* 8.4 Hz, ArH), 11.38 (br s, 1H, NH), 16.05 (br s, 1H, OH) ppm; ^{13}C NMR (DMSO-d_6, 50 MHz) δ 21.38, 21.96, 31.52, 34.04, 55.62, 113.13, 114.52, 121.13, 122.94, 127.38, 128.15, 128.76, 129.52, 133.41, 143.05, 147.11, 158.15 ppm; MS (EI, 70 eV): *m/z* 415 (26) [M^+], 303 (15), 275 (22), 274 (14), 260 (28), 227 (32), 174 (11), 173 (100), 172 (11), 171 (14), 143 (11), 118 (20), 117 (14), 116 (21), 115 (28), 103 (19%). Anal. Calcd for $C_{26}H_{29}N_3O_2$: C, 75.15; H, 7.03; N, 10.11. Found: C, 74.94; H, 7.50; N, 10.01.

2-((2-Amino-5-(*p*-tolyl)-1*H*-imidazol-4-yl)(4-methoxyphenyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone (10b). White powder of mp 175-177 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 0.95 (s, 6H, CH_3), 1.91-2.21 (m, 4H, CH_2), 2.28 (s, 3H, CH_3), 3.64 (s, 3H, OCH_3), 5.87 (s, 1H, CH), 6.40 (br s, 2H, NH_2), 6.72 (d, 2H, *J* 8.2 Hz, ArH), 6.92 (d, 2H, *J* 8.2 Hz, ArH), 7.18 (d, 2H, *J* 8.0 Hz, ArH), 7.30 (d, 2H, *J* 8.0 Hz, ArH), 11.34 (br s, 1H, NH), 16.15 (br s, 1H, OH) ppm; MS (EI, 70 eV): *m/z* 432 (10) [M^+], 431 (45), 430 (13), 346 (15), 319 (30), 292 (20), 291 (32), 290 (18), 260 (14), 258 (22), 257 (37), 234 (14), 227 (25), 174 (32), 173 (100), 172 (28), 171 (15%). Anal. Calcd for $C_{26}H_{29}N_3O_3$: C, 72.37; H, 6.67; N, 9.74. Found: C, 72.28; H, 6.54; N, 9.64.

2-((2-Amino-5-(*p*-tolyl)-1*H*-imidazol-4-yl)(4-chlorophenyl)methyl)-3-hydroxy-5,5-dimethyl cyclohex-2-enone (10c). White powder of mp 208-210 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 0.94 (s, 6H, CH_3), 2.00-2.18 (m, 4H, CH_2), 2.28 (s, 3H, CH_3), 5.89 (s, 1H, CH), 6.55 (br s, 2H, NH_2), 7.01 (d, 2H, *J* 8.4 Hz, ArH), 7.14-7.35 (m, 6H, ArH), 11.00 (br s, 1H, NH), 15.96 (br s, 1H, OH) ppm; MS (EI, 70 eV): *m/z* 436 (21) [M^+], 435 (48), 347 (27), 326 (33), 263 (100), 172 (42%). Anal. Calcd for $C_{25}H_{26}ClN_3O_2$: C, 68.88; H, 6.01; N, 9.64. Found: C, 68.78; H, 5.89; N, 9.50.

2-((2-Amino-5-(*p*-tolyl)-1*H*-imidazol-4-yl)(4-bromophenyl)methyl)-3-hydroxy-5,5-dimethyl cyclohex-2-enone (10d). White powder of mp 251-252 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 0.94 (s, 6H, CH_3), 2.09-2.15 (m, 4H, CH_2), 2.28 (s, 3H, CH_3), 5.89 (s, 1H, CH), 6.56 (br s, 2H, NH_2), 6.96 (d, 2H, *J* 8.4 Hz, ArH), 7.19 (d, 2H, *J* 7.9 Hz, ArH), 7.26-7.38 (m, 4H, ArH), 11.27 (br s, 1H, NH), 15.90 (br s, 1H, OH) ppm; ^{13}C NMR (DMSO-d_6, 50 MHz) δ 21.12, 21.68, 31.86, 32.83, 33.97, 34.13, 35.25, 112.97, 118.90, 121.14, 126.91, 127.43, 129.68, 130.03, 131.29, 131.41, 136.98, 144.73, 147.54 ppm; MS (EI, 70 eV): *m/z* 481 (18) [M^+], 479 (18), 260 (15), 174 (16), 173 (100), 172 (14), 171 (22), 117 (12), 116 (20), 115 (22), 84 (12), 83 (17), 56 (12), 55 (15%). Anal. Calcd for $C_{25}H_{26}BrN_3O_2$: C, 62.50; H, 5.46; N, 8.75. Found: C, 62.21; H, 6.52; N, 8.90.

2-((2-Amino-5-(*p*-tolyl)-1*H*-imidazol-4-yl)(phenyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone (10e). White powder of mp 225-226 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 0.96 (s, 6H, CH_3), 2.08-2.14 (m, 4H, CH_2), 2.28 (s, 3H, CH_3), 5.95 (s, 1H, CH), 6.42 (br s, 2H, NH_2), 6.98-7.03 (m, 3H, ArH), 7.10-7.22 (m, 4H, ArH), 7.32 (d, 2H, *J* 7.9 Hz, ArH), 11.29 (br s, 1H, NH), 15.93 (br s, 1H, OH) ppm; ^{13}C NMR (DMSO-d_6, 50 MHz) δ 31.85, 113.22, 120.93, 127.72, 130.72, 136.72, 145.10, 147.57 ppm; MS (EI, 70 eV): *m/z* 401 (64) [M^+], 345 (37), 324 (15), 317 (37), 316 (73), 290 (24), 289 (100), 288 (21), 275 (11), 274 (18), 262 (33), 261 (25), 260 (24), 228 (28), 227 (46), 174 (13), 173 (54), 144 (18), 131 (28), 130 (49%). Anal. Calcd for $C_{25}H_{27}N_3O_2$: C, 74.79; H, 6.78; N, 10.47. Found: C, 74.50; H, 8.02; N, 10.50.

2-((2-Amino-5-(*p*-tolyl)-1*H*-imidazol-4-yl)(4-carbmethoxyphenyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone (10f). White powder of mp 234-235 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 0.94 (s, 6H, CH_3), 2.06-2.12 (m, 4H, CH_2), 2.27 (s, 3H, CH_3), 3.78 (s, 3H, OCH_3), 5.99 (s, 1H, CH), 6.61 (br s, 2H, NH_2), 7.12-7.22 (m, 4H, ArH), 7.30 (d, 2H, *J* 7.9 Hz, ArH), 7.77 (d, 2H, *J* 8.1 Hz, ArH), 11.33 (br s, 1H, NH), 16.01 (br s, 1H, OH) ppm; ^{13}C NMR (DMSO-d_6, 50 MHz) δ 21.13, 21.67, 31.89, 34.83, 52.21, 112.91, 121.31, 127.40, 129.31, 129.79, 137.02, 147.53, 151.29, 166.86 ppm; MS (EI, 70 eV): *m/z* 459 (40) [M^+], 271 (37), 260 (13), 227 (10), 174 (24), 173 (100), 171 (20), 144 (16), 143 (22), 129 (12), 118 (21), 115 (15%). Anal. Calcd for $C_{27}H_{29}N_3O_4$: C, 70.57; H, 6.36; N, 9.14. Found: C, 70.31; H, 7.60; N, 9.32.

2-((2-Amino-5-(*p*-tolyl)-1*H*-imidazol-4-yl)(3,4-dimethoxyphenyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone (10g). White powder of mp 180-182 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 0.97 (s, 6H, CH_3), 2.08-2.21 (m, 4H, CH_2), 2.28 (s, 3H, CH_3), 3.56 (s, 3H, OCH_3), 3.64 (s, 3H, OCH_3), 5.86 (s, 1H, CH), 6.40 (br s, 2H, NH_2), 6.51 (dd, 1H, *J* 8.4 and 1.8 Hz, ArH), 6.63 (d, 1H, *J* 1,8 Hz, ArH), 6.74 (d, 1H, 8.4 Hz, ArH), 7.18 (d, 2H, *J* 8.3 Hz, ArH), 7.32 (d, 2H, *J* 8.3 Hz, ArH), 11.29 (br s, 1H, NH), 16.09 (br s, 1H, OH) ppm; MS (EI, 70 eV): *m/z* 462 (15) [M^+], 461 (50), 460 (12), 372 (19), 371 (34), 370 (23), 322 (100%). Anal. Calcd for $C_{27}H_{31}N_3O_4$: C, 70.26; H, 6.77; N, 9.10. Found: C, 70.16; H, 6.60; N, 9.00.

2-((2-Amino-5-(4-methoxyphenyl)-1*H*-imidazol-4-yl)(*p*-tolyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone (10h). White powder of mp 223-224 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 0.94 (s, 6H, CH_3), 2.05-2.11 (m, 4H, CH_2), 2.17 (s, 3H, CH_3), 3.73 (s, 3H, OCH_3), 5.84 (s, 1H, CH), 6.49 (br s, 2H, NH_2), 6.85-7.00 (m, 6H, ArH), 7.32 (d, 2H, *J* 8.6 Hz, ArH), 11.25 (br s, 1H, NH), 15.95 (br s, 1H, OH) ppm; ^{13}C NMR (DMSO-d_6, 50 MHz) δ 20.96, 31.61, 33.87, 55.62, 113.33, 114.71, 120.43, 122.87, 127.18, 128.14, 128.76, 129.50, 134.41, 142.05, 147.10, 158.65 ppm; MS (EI, 70 eV): *m/z*431 (17) [M^+], 375 (34), 374 (21), 341 (46), 325 (31), 324 (26), 293 (12), 292 (24), 291 (15), 243 (20), 241 (33), 189 (100), 188 (25%). Anal. Calcd for $C_{26}H_{29}N_3O_3$: C, 72.37; H, 6.77; N, 9.74. Found: C, 72.21; H, 7.09; N, 9.93.

2-((2-Amino-5-(4-methoxyphenyl)-1*H*-imidazol-4-yl)(4-methoxyphenyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone (10i). White powder of mp 215-216 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 0.94 (s, 6H, CH_3), 2.05-2.11 (m, 4H, CH_2), 3.64 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3), 5.83 (s, 1H, CH), 6.47 (br s, 2H, NH_2), 6.71 (d, 2H, *J* 8.6 Hz, ArH), 6.88-7.00 (m, 4H, ArH), 7.33 (d, 2H, *J* 8.2 Hz, ArH), 11.23 (br s, 1H, NH), 15.94 (br s, 1H, OH) ppm; ^{13}C NMR (DMSO-

d$_6$, 50 MHz) δ 31.81, 33.77, 55.64, 55.94, 113.36, 114.91, 121.43, 123.87, 127.24, 128.15, 128.82, 129.37, 135.41, 142.15, 147.17, 158.75 ppm; MS (EI, 70 eV): *m/z* 447 (16) [M$^+$], 343 (14), 342 (12), 340 (36), 310 (21), 309 (17), 308 (15), 261 (44), 260 (26), 189 (100), 140 (12%). Anal. Calcd for $C_{26}H_{29}N_3O_4$: C, 69.78; H, 6.53; N, 9.39. Found: C, 69.50; H, 6.87; N, 9.35.

2-((2-Amino-5-(4-methoxyphenyl)-1*H*-imidazol-4-yl)(4-chlorophenyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone (10J). White powder of mp 200-201 °C; ^{1}H NMR (DMSO-*d*$_6$, 200 MHz) δ 0.94 (s, 6H, CH_3), 2.05-2.11 (m, 4H, CH_2), 3.74 (s, 3H, OCH_3), 5.87 (s, 1H, CH), 6.63 (br s, 2H, NH_2), 6.92-7.06 (m, 4H, ArH), 7.22 (d, 2H, *J* 8.6 Hz, ArH), 7.33 (d, 2H, *J* 8.6 Hz, ArH), 11.25 (br s, 1H, NH), 15.85 (br s, 1H, OH) ppm; ^{13}C NMR (DMSO-*d*$_6$, 50 MHz) δ 31.65, 33.72, 55.64, 112.67, 114.77, 120.76, 122.51, 128.14, 128.28, 128.75, 129.04, 130.21, 144.19, 147.10, 158.82 ppm; MS (EI, 70 eV): *m/z* 451 (13) [M$^+$], 395 (16), 394 (14), 345 (22), 341 (15), 313 (12), 312 (14), 311 (21), 264 (33), 263 (13), 262 (17), 189 (100), 188 (17%). Anal. Calcd for $C_{25}H_{26}ClN_3O_3$: C, 66.44; H, 5.80; N, 9.30. Found: C, 66.35; H, 6.10; N, 9.22.

2-((2-Amino-5-(4-methoxyphenyl)-1*H*-imidazol-4-yl)(4-bromophenyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone (10k). White powder of mp 248-250 °C; ^{1}H NMR (DMSO-*d*$_6$, 200 MHz) δ 0.94 (s, 6H, CH_3), 2.06-2.11 (m, 4H, CH_2), 3.74 (s, 3H, OCH_3), 5.85 (s, 1H, CH), 6.65 (br s, 2H, NH_2), 6.92-7.02 (m, 4H, ArH), 7.29-7.42 (m, 4H, ArH), 11.36 (br s, 1H, NH), 15.84 (br s, 1H, OH) ppm; ^{13}C NMR (DMSO-*d*$_6$, 50 MHz) δ 21.68, 31.77, 33.87, 55.68, 113.17, 118.16, 121.24, 125.91, 127.05, 129.36, 131.03, 131.28, 135.98, 144.79, 148.54 ppm; MS (EI, 70 eV): *m/z* 497 (15), 495 (15) [M$^+$], 440 (16), 390 (14), 388 (14), 355 (17), 354 (15), 341 (12), 340 (13), 309 (18), 307 (18), 189 (100), 141 (22), 139 (19%). Anal. Calcd for $C_{25}H_{26}BrN_3O_3$: C, 60.49; H, 5.28; N, 8.47. Found: C, 60.25; H, 5.26; N, 8.24.

2-((2-Amino-5-(4-methoxyphenyl)-1*H*-imidazol-4-yl)(phenyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone (10l). White powder of mp 211-213 °C; ^{1}H NMR (DMSO-*d*$_6$, 200 MHz) δ 0.95 (s, 6H, CH_3), 2.05-2.12 (m, 4H, CH_2), 3.73 (s, 3H, OCH_3), 5.90 (s, 1H, CH), 6.54 (br s, 2H, NH_2), 6.92-7.07 (m, 5H, ArH), 7.10-7.19 (m, 2H, ArH), 7.35 (d, 2H, *J* 8.6 Hz, ArH), 11.28 (br s, 1H, NH), 15.85 (br s, 1H, OH) ppm; ^{13}C NMR (DMSO-*d*$_6$, 50 MHz) δ 31.63, 34.19, 55.64, 112.90, 114.75, 120.51, 122.28, 125.60, 127.25, 128.14, 129.54, 145.03, 147.14, 158.68 ppm; MS (EI, 70 eV): *m/z* 417 (18) [M$^+$], 362 (19), 361 (22), 360 (14), 341 (24), 340 (11), 339 (27), 309 (16), 278 (21), 277 (13), 231 (16), 230 (43), 229 (18), 189 (100), 188 (16), 140 (13%). Anal. Calcd for $C_{25}H_{27}N_3O_3$: C, 71.92; H, 6.52; N, 10.06. Found: C, 71.64; H, 6.83; N, 10.01.

2-((2-Amino-5-(4-methoxyphenyl)-1*H*-imidazol-4-yl)(4-carbmethoxyphenyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone (10m). White powder of mp 238-240 °C; ^{1}H NMR (DMSO-*d*$_6$, 200 MHz) δ 0.94 (s, 6H, CH_3), 2.06-2.11 (m, 4H, CH_2), 3.74 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 5.95 (s, 1H, CH), 6.69 (br s, 2H, NH_2), 6.96 (d, 2H, *J* 8.8 Hz, ArH), 7.15 (d, 2H, *J* 8.2 Hz, ArH), 7.33 (d, 2H, *J* 8.8 Hz, ArH), 7.77 (d, 2H, *J* 8.2 Hz, ArH), 11.30 (br s, 1H, NH), 15.70 (br s, 1H, OH) ppm; ^{13}C NMR (DMSO-*d*$_6$, 50 MHz) δ 21.67, 32.19, 34.73, 52.27, 55.94, 113.01, 121.44, 128.40, 129.21, 129.80, 167.92, 148.36, 152.29, 165.86 ppm; MS (EI, 70 eV): *m/z* 475 (15) [M$^+$], 420 (14) 419 (23), 369 (17), 368 (45), 342 (17), 341 (29), 337 (13), 336 (15),

335 (32), 189 (100), 187 (26), 139 (17), 136 (15%). Anal. Calcd for $C_{27}H_{29}N_3O_5$: C, 68.19; H, 6.15; N, 8.84. Found: C, 67.93; H, 6.41; N, 9.01.

2-((2-Amino-5-(4-bromophenyl)-1*H*-imidazol-4-yl)(*p*-tolyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone (10n). White powder of mp 230-232 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 0.94 (s, 6H, CH_3), 2.05-2.15 (m, 4H, CH_2), 2.17 (s, 3H, CH_3), 5.87 (s, 1H, CH), 6.42 (br s, 2H, NH_2), 6.89 (d, 2H, *J* 8.4 Hz, ArH), 6.97 (d, 2H, *J* 8.4 Hz, ArH), 7.34 (d, 2H, *J* 8.6 Hz, ArH), 7.58 (d, 2H, *J* 8.6 Hz, ArH), 11.27 (br s, 1H, NH), 16.11 (br s, 1H, OH) ppm; ^{13}C NMR (DMSO-d_6, 50 MHz) δ 21.05, 28.85, 31.67, 34.88, 48.97, 114.32, 119.88, 120.15, 127.51, 128.66, 129.00, 130.47, 132.23, 133.61, 134.86, 141.68, 148.78 ppm; MS (EI, 70 eV): *m/z* 481 (18) [M^+], 480 (11), 479 (18), 369 (33), 368 (21), 367 (32), 341 (18), 340 (28), 339 (17), 326 (18), 325 (13), 324 (23), 242 (14), 241 (29), 240 (14), 239 (44), 238 (21), 237 (44), 228 (18), 227 (100), 226 (20), 218 (17), 171 (32), 158 (29), 157 (30), 156 (12%). Anal. Calcd for $C_{25}H_{26}BrN_3O_2$: C, 62.50; H, 5.46; N, 8.75. Found: C, 62.42; H, 5.34; N, 8.64.

General procedure for the synthesis of 5-(1-(2-Amino-1*H*-imidazol-4-yl)methyl)-6-hydroxy-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-diones (12a-l)

Equimolar mixture (1 mmol) of 2-amino-4-arylimidadoze **1a,b**, 1,3-dimethylbarbituric acid **11,** the appropriate aromatic aldehyde **6a-h** in 2 mL of ethanol was placed in a 5 mL round-bottom flask equipped with a condenser and ultrasonicated in the ultrasonic bath at room temperature for 30-45 min. The precipitate formed was collected by filtration, washed with EtOH and dried at room temperature to produce compounds **12a-l**.

5-((2-Amino-5-(*p*-tolyl)-1*H*-imidazol-4-yl)(*p*-tolyl)methyl)-6-hydroxy-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (12a). White powder of mp 226-227 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 2.19 (s,3H, CH_3), 2.30 (s,3H, CH_3), 3.09 (s, 6H, CH_3), 5.79 (s, 1H, CH), 6.90 (d, 2H, *J* 8.2 Hz, ArH), 6.98 (d, 2H, *J* 8.2 Hz, ArH), 7.23 (d, 2H, *J* 7.9 Hz, ArH), 7.34 (br s, 2H, NH_2), 7.41 (d, 2H, *J* 7.9 Hz, ArH), 12.07 (br s, 1H, NH), 12.95 (br s, 1H, OH) ppm; ^{13}C NMR (DMSO-d_6, 50 MHz) δ 21.28, 21.56, 28.11, 35.08, 87.61, 121.94, 125.25, 126.75, 127.66, 128.45, 129.28, 130.18, 130.64, 138.35, 143.54, 146.73, 153.12, 164.00; MS (EI, 70 eV): *m/z* 431 (5) [M^+], 276 (20), 275 (85), 274 (33), 261 (16), 260 (85), 258 (13), 257 (22), 243 (12), 218 (21), 173 (22), 157 (13), 156 (84), 143 (11), 131 (20), 130 (24), 129 (15), 128 (12), 118 (25), 116 (25), 115 (33), 104 (14), 103 (26%). Anal. Calcd for $C_{24}H_{25}N_5O_3$: C, 66.81; H, 5.84; N, 16.23. Found: C, 65.89; H, 6.60; N, 15.84.

5-((2-Amino-5-(*p*-tolyl)-1*H*-imidazol-4-yl)(4-methoxyphenyl)methyl)-6-hydroxy-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (12b). White powder of mp 231-232 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 2.30 (s,3H, CH_3), 3.10 (s, 6H, CH_3), 3.65 (s,3H, OCH_3), 5.78 (s, 1H, CH), 6.74 (d, 2H, *J* 8.8 Hz, ArH), 6.93 (d, 2H, *J* 8.8 Hz, ArH), 7.24 (d, 2H, *J* 8.1 Hz, ArH), 7.36 (br s, 2H, NH_2), 7.42 (d, 2H, *J* 8.1 Hz, ArH), 12.10 (br s, 1H, NH), 13.01 (br s, 1H, OH) ppm; ^{13}C NMR (DMSO-d_6, 50 MHz) δ 21.15, 27.94, 34.88, 55.98, 87.62, 115.13, 121.24, 121.83, 128.12, 127.18, 129.13, 129.28, 134.85, 141.46, 145.37, 153.26, 159.80, 164.00; MS (EI, 70 eV): *m/z* 447 (10) [M^+], 354 (22), 341 (50), 340 (39), 339 (48), 293 (15), 292 (21), 261 (18), 260

(47), 173 (68), 156 (100), 107 (24%). Anal. Calcd for $C_{24}H_{25}N_5O_4$: C, 64.42; H, 5.63; N, 15.65. Found: C, 64.03; H, 6.12; N, 15.68.

5-((2-Amino-5-(*p*-tolyl)-1*H*-imidazol-4-yl)(4-chlorophenyl)methyl)-6-hydroxy-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (12c). White powder of mp 235-237 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 2.30 (s,3H, CH_3), 3.11 (s, 6H, CH_3), 5.81 (s, 1H, CH), 7.02 (d, 2H, *J* 8.6 Hz, ArH), 7.21-7.26 (m, 4H, ArH), 7.40 (br s, 2H, NH_2), 7.42 (d, 2H, *J* 8.6 Hz, ArH), 12.77 (br s, 1H, NH), 12.79 (br s, 1H, OH) ppm; ^{13}C NMR (DMSO-d_6, 50 MHz) δ 21.38, 28.01, 34.98, 87.41, 121.74, 126.25, 126.83, 127.66, 128.43, 129.18, 130.08, 130.74, 138.15, 143.46, 146.70, 153.16, 163.94; MS (EI, 70 eV): *m/z* 451 (24) [M], 298 (19), 297 (50), 296 (60), 294 (32), 277 (13), 260 (22), 238 (12), 218 (12), 178 (16), 173 (65), 156 (76), 151 (31), 150 (19), 118 (31), 116 (41%). Anal. Calcd for $C_{23}H_{22}ClN_5O_3$: C, 61.13; H, 4.91; N, 15.50. Found: C, 61.02; H, 4.85; N, 15.38.

5-((2-Amino-5-(*p*-tolyl)-1*H*-imidazol-4-yl)(4-bromophenyl)methyl)-6-hydroxy-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (12d). White powder of mp 246-247 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 2.30 (s,3H, CH_3), 3.10 (s, 6H, CH_3), 5.78 (s, 1H, CH), 6.97 (d, 2H, *J* 8.2 Hz, ArH), 7.25 (d, 2H, *J* 8.2 Hz, ArH), 7.34-7.46 (m, 6H, ArH+NH_2), 12.08 (br s, 1H, NH), 12.78 (br s, 1H, OH) ppm; ^{13}C NMR (DMSO-d_6, 50 MHz) δ 21.69, 27.98, 35.56, 87.87, 115.33, 121.24, 121.73, 127.93, 128.24, 129.24, 135.21, 145.93, 146.56, 153.62, 159.91, 164.00; MS (EI, 70 eV): *m/z* 497 (5), 495 (5) [M^+], 341 (75), 340 (44), 339 (73), 324 (40), 323 (48), 261 (15), 260 (73), 218 (18), 197 (20), 196 (19), 173 (70), 156 (100), 130 (39), 129 (24), 118 (33), 116 (29), 102 (15%). Anal. Calcd for $C_{23}H_{22}BrN_5O_3$: C, 55.65; H, 4.47; N, 14.11. Found: C, 55.23; H, 5.21; N, 14.12.

5-((2-Amino-5-(*p*-tolyl)-1*H*-imidazol-4-yl)(phenyl)methyl)-6-hydroxy-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (12e). White powder of mp 224-225 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 2.28 (s,3H, CH_3), 3.10 (s, 6H, CH_3), 5.84 (s, 1H, CH), 6.97-7.10 (m, 3H, ArH), 7.13-7.27 (m, 4H, ArH), 7.34 (br s, 2H, NH_2), 7.43 (d, 2H, *J* 8.1 Hz, ArH), 12.17 (br s, 1H, NH), 12.90 (br s, 1H, OH) ppm; ^{13}C NMR (DMSO-d_6, 50 MHz) δ 21.72, 27.95, 35.09, 87.54, 97.29, 121.68, 126.44, 126.93, 127.40, 127.65, 128.54, 130.07, 137.97, 144.16, 146.52, 153.07, 163.36; MS (EI, 70 eV): *m/z* 417 (3) [M^+], 261 (90), 260 (82), 244 (26), 243 (46), 186 (14), 173 (46), 156 (100), 131 (36), 130 (45), 118 (64), 117 (50), 103 (27), 102 (41%). Anal. Calcd for $C_{23}H_{23}N_5O_3$: C, 66.17; H, 5.55; N, 16.78. Found: C, 66.02; H, 6.40; N, 16.92.

5-((2-Amino-5-(*p*-tolyl)-1*H*-imidazol-4-yl)(4-carbmethoxphenyl)methyl)-6-hydroxy-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (12f).

White powder of mp 242-243 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 2.28 (s,3H, CH_3), 3.09 (s, 6H, CH_3), 3.77 (s,3H, OCH_3), 5.85 (s, 1H, CH), 7.15 (d, 2H, *J* 8.2 Hz, ArH), 7.23 (d, 2H, *J* 8.5 Hz, ArH), 7.29 (br s, 2H, NH_2), 7.41 (d, 2H, *J* 8.2 Hz, ArH), 7.78 (d, 2H, *J* 8.5 Hz, ArH), 12.12 (br s, 1H, NH), 12.93 (br s, 1H, OH) ppm; ^{13}C NMR (DMSO-d_6, 50 MHz) δ 21.23, 27.86, 35.24, 52.37, 87.40, 125.83, 127.42, 129.46, 129.91, 146.56, 150.09, 152.88, 163.61, 166.68; MS (EI, 70 eV): *m/z* 319 (66), 318 (43), 288 (14), 287 (65), 260 (57), 173 (12), 156 (56), 131 (13), 130

(21), 129 (27), 103 (13), 101 (20%). Anal. Calcd for $C_{25}H_{25}N_5O_5$: C, 63.15; H, 5.30; N, 14.73. Found: C, 62.60; H, 5.80; N, 14.40.

5-((2-Amino-5-(4-methoxyphenyl)-1*H*-imidazol-4-yl)(*p*-tolyl)methyl)-6-hydroxy-1,3-dimethylpyrimi-dine-2,4(1*H*,3*H*)-dione (12g). White powder of mp 211-213 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 2.19 (s, 3H, CH_3), 3.10 (s, 6H, CH_3), 3.77 (s, 3H, OCH_3), 5.76 (s, 1H, CH), 6,90 (d, 2H, *J* 8.2 Hz, ArH), 6.98 (d, 2H, *J* 8.2 Hz, ArH), 7.01 (d, 2H, *J* 8.6 Hz, ArH), 7.38 (br s, 2H, NH_2), 7.48 (d, 2H, *J* 8.6 Hz, ArH), 12.03 (br s, 1H, NH), 12.91 (br s, 1H, OH) ppm; ^{13}C NMR (DMSO-d_6, 50 MHz) δ 21.10, 27.99, 34.98, 56.00, 87.73, 115.13, 121.21, 121.73, 127.12, 127.28, 129.03, 129.18, 134.83, 141.44, 146.37, 153.21, 159.81, 163.97; MS (EI, 70 eV): *m/z* 448 (23) [M^+], 292 (21), 291 (100), 290 (30), 276 (23), 258 (15), 257 (22), 189 (20), 174 (11), 134 (12), 130 (13), 115 (12), 103 (16%). Anal. Calcd for $C_{24}H_{25}N_5O_4$: C, 64.42; H, 5.63; N, 15.65. Found: C, 64.33; H, 5.51; N, 15.57.

5-((2-Amino-5-(4-methoxyphenyl)-1*H*-imidazol-4-yl)(4-methoxyphenyl)methyl)-6-hydroxy-1,3-di-methylpyrimidine-2,4(1*H*,3*H*)-dione (12h). White powder of mp 233-235 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 3.10 (s, 6H, CH_3), 3.65 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 5.75 (s, 1H, CH), 6.74 (d, 2H, *J* 8.6 Hz, ArH), 6.93 (d, 2H, *J* 8.6 Hz, ArH), 7.01 (d, 2H, *J* 8.6 Hz, ArH), 7.34 (br s, 2H, NH_2), 7.47 (d, 2H, *J* 8.6 Hz, ArH), 12.05 (br s, 1H, NH), 12.93 (br s, 1H, OH) ppm; ^{13}C NMR (DMSO-d_6, 50 MHz) δ 28.00, 34.56, 55.76, 55.99, 87.68, 114.13, 115.14, 121.11, 121.71, 127.23, 128.34, 129.18, 136.43, 146.36, 153.19, 158.00, 159.79, 163.96; MS (EI, 70 eV): *m/z* 464 (19) [M^+], 463 (57) [M], 356 (12), 308 (24), 275 (34%). Anal. Calcd for $C_{24}H_{25}N_5O_5$: C, 62.19; H, 5.44; N, 15.11. Found: C, 62.08; H, 5.31; N, 15.01

5-((2-Amino-5-(4-methoxyphenyl)-1*H*-imidazol-4-yl)(4-chlorophenyl)methyl)-6-hydroxy-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (12i). White powder of mp 223-225 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 3.33 (s, 6H, CH_3), 3.77 (s, 3H, OCH_3), 5.77 (s, 1H, CH), 6.96-7.05 (m, 4H, ArH), 7.24 (d, 2H, *J* 8.4 Hz, ArH), 7.38 (br s, 2H, NH_2), 7.47 (d, 2H, *J* 8.6 Hz, ArH), 12.11 (br s, 1H, NH), 12.68 (br s, 1H, OH) ppm; ^{13}C NMR (DMSO-d_6, 50 MHz) δ 27.98, 34.99, 56.02, 87.41, 115.22, 121.53, 121.62, 126.31, 128.39, 129.20, 129.27, 130.72, 143.55, 146.56, 153.20, 159.93, 163.96; MS (EI, 70 eV): *m/z* 468 (20), 467 (51) [M], 360 (27), 280 (17), 279 (71), 188 (25%). Anal. Calcd for $C_{23}H_{22}ClN_5O_4$: C, 59.04; H, 4.74; N, 14.97. Found: C, 58.90; H, 4.65; N, 14.89.

5-((2-Amino-5-(4-methoxyphenyl)-1*H*-imidazol-4-yl)(4-bromophenyl)methyl)-6-hydroxy-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (12J). White powder of mp 268-270 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 3.10 (s, 6H, CH_3), 3.76 (s, 3H, OCH_3), 5.75 (s, 1H, CH), 6.95-7.04 (m, 4H, ArH), 7.36 (br s, 2H, NH_2), 7.37 (d, 2H, *J* 8.6 Hz, ArH), 7.46 (d, 2H, *J* 8.6 Hz, ArH), 12.10 (br s, 1H, NH), 12.68 (br s, 1H, OH) ppm; ^{13}C NMR (DMSO-d_6, 50 MHz) δ 28.00, 35.46, 56.06, 87.66, 115.14, 121.19, 121.73, 127.73, 128.36, 129.24, 135.11, 145.73, 146.36, 153.22, 159.71, 164.00; MS (EI, 70 eV): *m/z* 512 (16) [M^+], 511 (39) [M], 357 (11), 356 (23), 325 (17), 324 (13%). Anal. Calcd for $C_{23}H_{22}BrN_5O_4$: C, 53.92; H, 4.33; N, 13.67. Found: C, 53.81; H, 4.20; N, 13.58.

5-((2-Amino-5-(4-methoxyphenyl)-1*H*-imidazol-4-yl)(phenyl)methyl)-6-hydroxy-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (12k). White powder of mp 206-208 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 3.11 (s, 6H, CH_3), 3.76 (s, 3H, OCH_3), 5.82 (s, 1H, CH), 6.97-7.22 (m, 7H, ArH), 7.36 (br s, 2H, NH_2), 7,49 (d, 2H, *J* 8.6 Hz, ArH), 12.08 (br s, 1H, NH), 12.86 (br s, 1H, OH) ppm; ^{13}C NMR (DMSO-d_6, 50 MHz) δ 28.00, 35.31, 56.03, 87.54, 115.16, 121.39, 121.69, 125.96, 126.87, 127.35, 128.46, 129.32, 144.43, 146.42, 153.21, 159.83, 164.00; MS (EI, 70 eV): *m/z* 434 (15) [M^+], 433 (43) [M], 417 (12), 279 (18), 245 (29%). Anal. Calcd for $C_{23}H_{23}N_5O_4$: C, 63.73; H, 5.35; N, 16.16. Found: C, 63.62; H, 5.27; N, 16.07.

5-((2-Amino-5-(4-methoxyphenyl)-1*H*-imidazol-4-yl)(4-nitrophenyl)methyl)-6-hydroxy-1,3-dimethyl-pyrimidine-2,4(1*H*,3*H*)-dione (12l). White powder of mp 264-266 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 3.11 (s, 6H, CH_3), 3.75 (s, 3H, OCH_3), 5.87 (s, 1H, CH), 7.01 (d, 2H, *J* 8.6 Hz, ArH), 7.28 (d, 2H, *J* 8.6 Hz, ArH), 7.35 (br s, 2H, NH_2), 7.47 (d, 2H, *J* 8.6 Hz, ArH), 8.07 (d, 2H, *J* 8.6 Hz, ArH), 12.40 (br s, 1H, NH), 12.98 (br s, 1H, OH) ppm; ^{13}C NMR (DMSO-d_6, 50 MHz) δ 28.05, 35.34, 56.08, 87.74, 115.16, 121.29, 121.74, 126.77, 127.45, 128.46, 129.22, 145.43, 146.38, 153.22, 159.73, 164.00; MS (EI, 70 eV): *m/z* 479 (13) [M^+], 478 (43) [M], 371 (16), 323 (27), 290 (63), 188 (24). Anal. Calcd for $C_{23}H_{22}N_6O_6$: C, 57.74; H, 4.63; N, 17.56. Found: C, 57.65; H, 4.45; N, 17.43.

5-(4-Fluorophenyl)-2,7-di-(*p*-tolyl)imidazo[1,2-*a*] pyrimidine (13a). Yellow powder of mp 265-267 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 2.35 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 7.31-7.48 (m, 4H, ArH), 7.53-7.65 (m, 2H, ArH), 7.97-8.08 (m, 4H, ArH), 8.21 (s, 1H, 6-CH), 8.33 (d, 2H, *J* 8.3 Hz, ArH), 8.59 (s, 1H, 3-CH) ppm; MS (EI, 70 eV): *m/z* 396 (28) [M^+], 395 (100), 394 (52), 393 (52), 392 (21), 301 (15), 300 (62), 273 (31), 272 (11%). Anal. Calcd for $C_{26}H_{20}FN_3$: C, 79.37; H, 5.12; N, 10.68. Found: C, 79.26; H, 5.01; N, 10.50.

2-(4-Bromophenyl)-5-phenyl-7-(*p*-tolyl)imidazo[1,2-*a*]pyrimidine (13b). Yellow crystals of mp 277-279 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 2.38 (s, 3H, CH_3), 7.36 (d, 2H, *J* 8.4 Hz, ArH), 7.62 (d, 2H, *J* 8.6 Hz, ArH), 7.65-7.70 (m, 3H, ArH), 7.71 (s, 1H, 6-CH), 7.92-7.98 (m, 2H, ArH), 8.05 (d, 2H, *J* 8.6 Hz, ArH), 8.23 (d, 2H, *J* 8.4 Hz, ArH), 8.40 (s, 1H, 3-CH) ppm; ^{13}C NMR (DMSO-d_6, 50 MHz) δ 21.54, 106.39, 121.96, 127.83, 128.65, 129.09, 129.98, 130.14, 131.54, 132.20, 132.81, 133.64, 135.04, 141.04, 145.96, 146.62, 150.15, 157.04; MS (EI, 70 eV): *m/z* 442 (26), 441 (98) [M^+], 440 (70), 439 (100), 438 (45), 360 (16%). Anal. Calcd for $C_{25}H_{18}BrN_3$: C, 68.19; H, 4.12; N, 9.54. Found: C, 68.07; H, 4.01; N, 9.38.

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