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

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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, ultrasound-assisted synthesis

Introduction

2-Amino-1H-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 aminimidazole moiety display a broad range of biological properties and were recognized as H1- and H2-receptor agonists and antagonists,2 5-HT3 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-1H-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).\(^7\)

\[
\begin{align*}
\text{R}^1\text{O} + \text{R}^2\text{CO}R^3 & \rightarrow \\
\begin{array}{c}
\text{N} \\
\text{N} \\
\text{H} \\
\text{H} \\
\end{array}
\end{align*}
\]

\[
\begin{align*}
\text{1} & \rightarrow \\
\begin{array}{c}
\text{R}^1 \text{C} \text{O} \text{R}^2 \\
\text{R}^1 \text{C} \text{O} \text{R}^2 \\
\text{R}^1 \text{C} \text{O} \text{R}^2 \\
\text{R}^1 \text{C} \text{O} \text{R}^2 \\
\end{array}
\end{align*}
\]

\[
\begin{align*}
\text{R}^1 \text{C} \text{O} \text{R}^2 & \rightarrow \\
\begin{array}{c}
\text{R}^1 \text{C} \text{O} \text{R}^2 \\
\text{R}^1 \text{C} \text{O} \text{R}^2 \\
\text{R}^1 \text{C} \text{O} \text{R}^2 \\
\text{R}^1 \text{C} \text{O} \text{R}^2 \\
\end{array}
\end{align*}
\]

\[
\begin{align*}
\text{R}^1 \text{C} \text{O} \text{R}^2 & \rightarrow \\
\begin{array}{c}
\text{R}^1 \text{C} \text{O} \text{R}^2 \\
\text{R}^1 \text{C} \text{O} \text{R}^2 \\
\text{R}^1 \text{C} \text{O} \text{R}^2 \\
\text{R}^1 \text{C} \text{O} \text{R}^2 \\
\end{array}
\end{align*}
\]

\[
\begin{align*}
\text{R}^1 \text{C} \text{O} \text{R}^2 & \rightarrow \\
\begin{array}{c}
\text{R}^1 \text{C} \text{O} \text{R}^2 \\
\text{R}^1 \text{C} \text{O} \text{R}^2 \\
\text{R}^1 \text{C} \text{O} \text{R}^2 \\
\text{R}^1 \text{C} \text{O} \text{R}^2 \\
\end{array}
\end{align*}
\]

\[\text{5} \rightarrow \text{2} \rightarrow \text{3} \rightarrow \text{4}\]

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

Other publication reported sequential reactions *via* preliminary synthesis of \(\alpha,\beta\)-unsaturated compounds. For example, it was described synthesis of 5,6-dihydroimidazo[1,2-\(a\)]pyrimidines \(3\) by reaction of aminomimidazoles \(1\) with chalcones.\(^8\)a 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.\(^8\)b-d In all the cases reported only one endocyclic nucleophilic center of aminooazole 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,\(^\text{6b,9}\) herein we report a three-component reaction of 4-aryl-2-amino-1H-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 dimesdone 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, H2O) and aprotic (DMF, toluene) solvents and several types of additives (Et3N, HCl, Ac2O, 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 Et3N 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.

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. 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 Et₃N 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. 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 (Et₃N) catalysts decreased yields and purity of the compounds 12.

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-c]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 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/Et3N, 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.


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 $\alpha,\beta$-unsaturated carbonyls.

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

<table>
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<tr>
<th>Compound</th>
<th>$R$</th>
<th>$R^1$</th>
<th>$R^2$</th>
<th>Yield%</th>
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<td>4-FC$_6$H$_4$</td>
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<tr>
<td>3b</td>
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<td>4-ClC$_6$H$_4$</td>
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<tr>
<td>3c</td>
<td>4-BrC$_6$H$_4$</td>
<td>4-MeOC$_6$H$_4$</td>
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<td>84</td>
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<tr>
<td>3d</td>
<td>4-BrC$_6$H$_4$</td>
<td>C$_6$H$_5$</td>
<td>4-MeC$_6$H$_4$</td>
<td>82</td>
</tr>
<tr>
<td>10a</td>
<td>4-MeC$_6$H$_4$</td>
<td>4-MeC$_6$H$_4$</td>
<td>-</td>
<td>73$^a$</td>
</tr>
<tr>
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<td>70$^a$</td>
</tr>
<tr>
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<td>-</td>
<td>72$^a$</td>
</tr>
<tr>
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<td>4-BrC$_6$H$_4$</td>
<td>-</td>
<td>84$^a$</td>
</tr>
<tr>
<td>10e</td>
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<td>-</td>
<td>72$^a$</td>
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<td>3,4-(MeO)$_2$C$_6$H$_3$</td>
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<tr>
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<td>74$^a$</td>
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<td>80$^a$</td>
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<tr>
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<td>4-MeC$_6$H$_4$</td>
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Table 1. Continued

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<th>Compound</th>
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<th>R²</th>
<th>Yield%</th>
</tr>
</thead>
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<td>4-MeOC₆H₄</td>
<td>-</td>
<td>82</td>
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<tr>
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<td>-</td>
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<tr>
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<td>4-BrC₆H₄</td>
<td>-</td>
<td>85</td>
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<tr>
<td>12e</td>
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<td>C₆H₅</td>
<td>-</td>
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<tr>
<td>12f</td>
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<td>4-COOMeC₆H₄</td>
<td>-</td>
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<td>4-MeC₆H₄</td>
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<td>4-MeOC₆H₄</td>
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<td>13b</td>
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<td>C₆H₅</td>
<td>4-MeC₆H₄</td>
<td>83</td>
</tr>
</tbody>
</table>

*a microwave-assisted procedure

Treatment of aryldienobarbituric acids 15a-d and aminimidazole 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 aryldencyclohexan-1,3-diones in addition we carried out reaction of aminimidazole 1a with compounds 16a-d which also led to formation of adducts 10a,b,d,e.

The difference between behavior of chalcones 8a or aryldien derivatives of acetoacetic acid esters 8b-d and cyclic α,β-unsaturated ketones 15a-d in their reaction with aminimidazoles 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 1 (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, 1H 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 CH₂ groups, singlet for two methyl groups (0.9 ppm), singlet for the NH₂ 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 dimeredone fragment with barbituric one.

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

**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$^{\text{TM}}$ 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$_3$H$_7$NO are triclinic. At 293 K $a = 10.439(2)$, $b = 13.997(2)$, $c = 20.769(3)$ Å, $\alpha = 75.29(1)^\circ$, $\beta = 87.48(1)^\circ$, $\gamma = 71.75(1)^\circ$, $V = 2763.5(7)$ Å$^3$, $M_r = 553.49$, $Z = 4$, space group $P\overline{1}$, $d_{calc}=1.330$ g/cm$^3$, $\mu$(MoK$_\alpha$) = 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$_\alpha$ radiation, CCD detector, $\omega$-scanning, $2\Theta_{max} = 60^\circ$). 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 $F>4\sigma(F)$, $S = 0.768$). 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 Et₃N 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/H₂O (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; ¹H NMR (DMSO-d₆, 200 MHz) δ 2.28 (s, 3H, CH₃), 2.35 (s, 3H, CH₃), 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), 7.63 (d, 2H, 8.9 Hz, ArH), 7.94 (d, 2H, 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 C₂₆H₂₂FN₃: 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; ¹H NMR (DMSO-d₆, 200 MHz) δ 2.33 (s, 3H, CH₃), 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 C₂₅H₁₉BrClN₃: 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; ¹H NMR (DMSO-d₆, 200 MHz) δ 2.27 (s, 3H, CH₃), 3.35-3.39 (m, 1H, 6-CH), 3.48-3.52 (m, 1H, 6-CH), 3.80 (s, 3H, OCH₃), 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 C₂₆H₂₂BrO: 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; ¹H NMR (DMSO-d₆, 200 MHz) δ 2.27 (s, 3H, CH₃), 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 C₂₅H₂₀BrN₃: 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-1H-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 Et₃N 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/H2O 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/H2O (1:1), and dried at room temperature to produce the adduct 10a-n.

2-((2-Amino-5-(p-tolyl)-1H-imidazol-4-yl)(p-tolyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone (10a). White powder of mp 195-196 ⁰C; ¹H NMR (DMSO-d6, 200 MHz) δ 0.94 (s, 6H, CH3), 2.06-2.13 (m, 4H, CH2), 2.18 (s, 3H, CH3), 2.27 (s, 3H, CH3), 5.89 (s, 1H, CH), 6.42 (br s, 2H, NH2), 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; ¹³C NMR (DMSO-d6, 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, 151.11, 151.85 ppm; MS (EI, 70 eV): m/z 432 (26) [M⁺], 293 (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 C26H29N3O2: 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)-1H-imidazol-4-yl)(4-methoxyphenyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone (10b). White powder of mp 175-177 ⁰C; ¹H NMR (DMSO-d6, 200 MHz) δ 0.95 (s, 6H, CH3), 1.91-2.21 (m, 4H, CH2), 2.28 (s, 3H, CH3), 3.64 (s, 3H, OCH3), 5.87 (s, 1H, CH), 6.40 (br s, 2H, NH2), 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 C26H29N3O3: 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)-1H-imidazol-4-yl)(4-chlorophenyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone (10c). White powder of mp 208-210 ⁰C; ¹H NMR (DMSO-d6, 200 MHz) δ 0.94 (s, 6H, CH3), 2.00-2.18 (m, 4H, CH2), 2.28 (s, 3H, CH3), 5.89 (s, 1H, CH), 6.55 (br s, 2H, NH2), 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 C25H26ClN3O2: 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)-1H-imidazol-4-yl)(4-bromophenyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone (10d). White powder of mp 251-252 ⁰C; ¹H NMR (DMSO-d6, 200 MHz) δ 0.94 (s, 6H, CH3), 2.09-2.15 (m, 4H, CH2), 2.28 (s, 3H, CH3), 5.89 (s, 1H, CH), 6.56 (br s, 2H, NH2), 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; ¹³C NMR (DMSO-d6, 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 C25H26BrN3O2: 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)-1H-imidazol-4-yl)(phenyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone (10e). White powder of mp 225-226 °C; 1H 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$_3$O$_2$: 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)-1H-imidazol-4-yl)(4-carbomethoxyphenyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone (10f). White powder of mp 234-235 °C; 1H 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, 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), 143 (14), 143 (22), 129 (12), 118 (21), 115 (15%). Anal. Calcd for C$_{27}$H$_{29}$N$_3$O$_4$: 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)-1H-imidazol-4-yl)(3,4-dimethoxyphenyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone (10g). White powder of mp 180-182 °C; 1H 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$_{27}$N$_3$O$_4$: 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)-1H-imidazol-4-yl)(p-tolyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone (10h). White powder of mp 223-224 °C; 1H 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$_3$O$_3$: 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)-1H-imidazol-4-yl)(4-methoxyphenyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone (10i). White powder of mp 215-216 °C; 1H 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) $\delta$ 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$_{3}$O$_{4}$: 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)-1H-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) $\delta$ 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) $\delta$ 31.65, 33.72, 55.64, 112.67, 114.77, 120.76, 122.51, 128.14, 128.75, 129.04, 130.21, 134.19, 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$_{3}$O$_{3}$: 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)-1H-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) $\delta$ 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) $\delta$ 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$_{3}$O$_{3}$: 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)-1H-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) $\delta$ 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) $\delta$ 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$_{3}$O$_{3}$: 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)-1H-imidazol-4-yl)(4-carbomethoxyphenyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone (10m). White powder of mp 238-240 °C; $^1$H NMR (DMSO-$d_6$, 200 MHz) $\delta$ 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) $\delta$ 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 (17), 334 (14), 333 (12), 332 (12), 331 (26), 330 (18), 295 (17), 294 (17), 293 (15), 292 (16), 291 (17), 290 (18), 289 (20), 288 (21), 287 (22), 286 (23), 285 (24), 284 (25).
335 (32), 189 (100), 187 (26), 139 (17), 136 (15%). Anal. Calcd for C_{27}H_{29}N_{3}O_{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)-1H-imidazol-4-yl(p-tolyl)methyl)-3-hydroxy-5,5-dimethylcyclohex-2-enone (10n). White powder of mp 230-232 °C; ^1H NMR (DMSO-\textit{d}_6, 200 MHz) δ 0.94 (s, 6H, CH\textsubscript{3}), 2.05-2.15 (m, 4H, CH\textsubscript{2}), 2.17 (s, 3H, CH\textsubscript{3}), 5.87 (s, 1H, CH), 6.42 (br s, 2H, NH\textsubscript{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; ^13C NMR (DMSO-\textit{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): \textit{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\textsubscript{25}H\textsubscript{26}BrN\textsubscript{2}O\textsubscript{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-1H-imidazol-4-yl)methyl)-6-hydroxy-1,3-dimethylpyrimidine-2,4(1H,3H)-diones (12a-l)

Equimolar mixture (1 mmol) of 2-aminobis-4-arylimidazoide 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)-1H-imidazol-4-yl)(p-tolyl)methyl)-6-hydroxy-1,3-dimethylpyrimidine-2,4(1H,3H)-dione (12a). White powder of mp 226-227 °C; ^1H NMR (DMSO-\textit{d}_6, 200 MHz) δ 2.19 (s,3H, CH\textsubscript{3}), 2.30 (s,3H, CH\textsubscript{3}), 3.09 (s, 6H, CH\textsubscript{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\textsubscript{2}), 7.41 (d, 2H, J 7.9 Hz, ArH), 12.07 (br s, 1H, NH), 12.95 (br s, 1H, OH) ppm; ^13C NMR (DMSO-\textit{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): \textit{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\textsubscript{24}H\textsubscript{25}N\textsubscript{5}O\textsubscript{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)-1H-imidazol-4-yl)(4-methoxyphenyl)methyl)-6-hydroxy-1,3-dimethylpyrimidine-2,4(1H,3H)-dione (12b). White powder of mp 231-232 °C; ^1H NMR (DMSO-\textit{d}_6, 200 MHz) δ 2.30 (s,3H, CH\textsubscript{3}), 3.10 (s, 6H, CH\textsubscript{3}), 3.65 (s,3H, OCH\textsubscript{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\textsubscript{2}), 7.42 (d, 2H, J 8.1 Hz, ArH), 12.10 (br s, 1H, NH), 13.01 (br s, 1H, OH) ppm; ^13C NMR (DMSO-\textit{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): \textit{m/z} 447 (10) [M^+], 354 (22), 341 (50), 340 (39), 339 (48), 293 (15), 292 (21), 261 (18), 260
5-(2-Amino-5-(p-tolyl)-1H-imidazol-4-yl)(4-chlorophenyl)methyl)-6-hydroxy-1,3-dimethylpyrimidine-2,4(1H,3H)-dione (12c). White powder of mp 235-237 °C; \(^1\)H NMR (DMSO-\(d_6\), 200 MHz) \(\delta\) 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; \(^1^3\)C NMR (DMSO-\(d_6\), 50 MHz) \(\delta\) 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\(_{27}\)ClN\(_5\)O\(_3\): 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)-1H-imidazol-4-yl)(4-bromophenyl)methyl)-6-hydroxy-1,3-dimethylpyrimidine-2,4(1H,3H)-dione (12d). White powder of mp 246-247 °C; \(^1\)H NMR (DMSO-\(d_6\), 200 MHz) \(\delta\) 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; \(^1^3\)C NMR (DMSO-\(d_6\), 50 MHz) \(\delta\) 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\(_{27}\)BrN\(_5\)O\(_3\): 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)-1H-imidazol-4-yl)(phenyl)methyl)-6-hydroxy-1,3-dimethylpyrimidine-2,4(1H,3H)-dione (12e). White powder of mp 224-225 °C; \(^1\)H NMR (DMSO-\(d_6\), 200 MHz) \(\delta\) 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; \(^1^3\)C NMR (DMSO-\(d_6\), 50 MHz) \(\delta\) 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\(_{27}\)N\(_5\)O\(_3\): 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)-1H-imidazol-4-yl)(4-carbomethoxophenyl)methyl)-6-hydroxy-1,3-dimethylpyrimidine-2,4(1H,3H)-dione (12f). White powder of mp 242-243 °C; \(^1\)H NMR (DMSO-\(d_6\), 200 MHz) \(\delta\) 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), 7.77 (d, 2H, J 8.5 Hz, ArH), 12.12 (br s, 1H, NH), 12.93 (br s, 1H, OH) ppm; \(^1^3\)C NMR (DMSO-\(d_6\), 50 MHz) \(\delta\) 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_{5}O_{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)-1H-imidazol-4-yl)(p-tolyl)methyl)-6-hydroxy-1,3-dimethylpyrimidine-2,4(1H,3H)-dione (12g). White powder of mp 211-213 °C; \(^1\)H NMR (DMSO-d\(_6\), 200 MHz) \(\delta\) 2.19 (s, 3H, CH\(_3\)), 3.10 (s, 6H, CH\(_2\)), 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) \(\delta\) 21.10, 27.99, 34.98, 56.00, 87.73, 115.13, 121.21, 121.73, 127.12, 127.28, 129.03, 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\(_5\)O\(_4\): 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)-1H-imidazol-4-yl)(4-methoxyphenyl)methyl)-6-hydroxy-1,3-di-methylpyrimidine-2,4(1H,3H)-dione (12h). White powder of mp 233-235 °C; \(^1\)H NMR (DMSO-d\(_6\), 200 MHz) \(\delta\) 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) \(\delta\) 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\(_{23}\)N\(_5\)O\(_4\): 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)-1H-imidazol-4-yl)(4-chlorophenyl)methyl)-6-hydroxy-1,3-di-methylpyrimidine-2,4(1H,3H)-dione (12i). White powder of mp 223-225 °C; \(^1\)H NMR (DMSO-d\(_6\), 200 MHz) \(\delta\) 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) \(\delta\) 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\(_5\)O\(_4\): 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)-1H-imidazol-4-yl)(4-bromophenyl)methyl)-6-hydroxy-1,3-di-methylpyrimidine-2,4(1H,3H)-dione (12j). White powder of mp 268-270 °C; \(^1\)H NMR (DMSO-d\(_6\), 200 MHz) \(\delta\) 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) \(\delta\) 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\(_5\)O\(_4\): 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)-1H-imidazol-4-yl)(phenyl)methyl)-6-hydroxy-1,3-dimethylpyrimidine-2,4(1H,3H)-dione (12k). White powder of mp 206-208 °C; $^1$H NMR (DMSO-$d_6$, 200 MHz) $\delta$ 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) $\delta$ 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$_{22}$N$_5$O$_4$: 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)-1H-imidazol-4-yl)(4-nitrophenyl)methyl)-6-hydroxy-1,3-dimethyl-pyrimidine-2,4(1H,3H)-dione (12l). White powder of mp 264-266 °C; $^1$H NMR (DMSO-$d_6$, 200 MHz) $\delta$ 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) $\delta$ 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$_5$O$_4$: 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-tolyi)imidazo[1,2-a]pyrimidine (13a). Yellow powder of mp 265-267 °C; $^1$H NMR (DMSO-$d_6$, 200 MHz) $\delta$ 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$_{20}$F$_2$N$_5$: 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-tolyi)imidazo[1,2-a]pyrimidine (13b). Yellow crystals of mp 277-279 °C; $^1$H NMR (DMSO-$d_6$, 200 MHz) $\delta$ 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) $\delta$ 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.

References

1. (a) Hoffmann, H.; Lindel, T. *Synthesis* 2003, 1753.
(b) Ralifo, P.; Tenney, K.; Valeriote, F. A.; Crews, P. *J. Nat. Prod.* 2007, 70, 33. [http://dx.doi.org/10.1021/np060462b](http://dx.doi.org/10.1021/np060462b); PMid:17253846.
(d) Muravyova, E. A.; Shishkina, S. V.; Musatov, V. I.; Knyazeva, I. V.; Shishkin, O. V.; Desenko, S. M.; Chebanov, V. A. Synthesis 2009, 1375.
(b) Hügel H. M. Molecules, 2009, 14, 4936.
   [http://dx.doi.org/10.1107/S0108767307043930](http://dx.doi.org/10.1107/S0108767307043930); PMid:18156677.