Microwave-assisted Synthesis of New Regioisomeric 6,7-Dihydroindeno[1,2-*e*]pyrimido[4,5-*b*][1,4]diazepin-5(5a*H*)-ones

Braulio Insuasty[a]*, Fabián Orozco[a], Angélica García[a], Jairo Quiroga[a], Rodrigo Abonía[a], [b]*, M. Nogueras and Justo Cobo[b]

[a]Heterocyclic Compounds Research Group, Department of Chemistry, Calle 13 No. 100-00 Meléndez, Universidad del Valle, A. A. 25360 Cali, Colombia

[b]Department of Inorganic and Organic Chemistry, Universidad de Jaén, 23071 Jaén, Spain

Corresponding authors e-mail: brainsu@univalle.edu.co and mmontiel@ujaen.es

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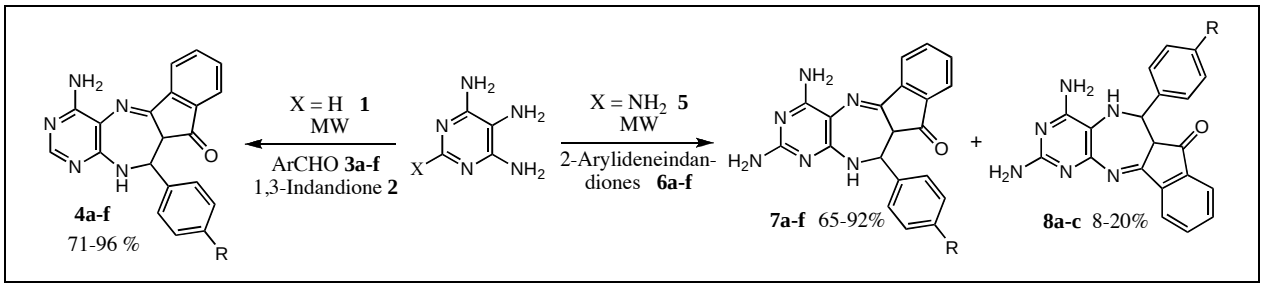

Novel 11-amino-6-aryl-6,7-dihydroindeno[1,2-*e*]pyrimido[4,5-*b*][1,4]diazepin-5(5a*H*)-ones **4a-f** were prepared regioselectively by the tricomponent reaction of 4,5,6-triaminopyrimidine **1**, 1,3-indandione **2** and aromatic aldehydes **3a-f**. The bicomponent approach, using 2,4,5,6-tetraaminopyrimidine **5** and 2-arylideneindandiones **6a-f** as reagents, afforded 9,11-diamino-6-aryl-6,7-dihydroindeno[1,2-*e*]pyrimido[4,5-*b*]-[1,4]diazepin-5(5a*H*)-ones **7a-f** in good yields and the regioisomeric 8,10-diamino derivatives **8a-c** in lower yields. Both, bi- and tricomponent approaches were performed by microwave irradiation and all products were fully characterized by detailed NMR measurements.

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INTRODUCTION

The biological activity of fused 1,4-diazepine systems has been emphasized largely in several reports [1-4]. Among the fused diazepine systems mentioned, those containing heterocycles attached to the seven-member ring, have shown important and varied bioactivities [5,6], which is also the case of pyrimido[4,5-*b*][1,4]diazepines successfully synthesized [7-9], and some of them found to be especially active against different cancer types, as described in one of our previous papers [10].

On the other hand, derivatives of 1,3-indandione have been related with interesting biological activities as antioxidants [11], anticoagulants [12], antibacterials [13-16] and CDK (Cyclin-Dependent Kinases) inhibitors [17,18]. This makes the combination of pyrimido-diazepine and indeno moieties synthetically as well as pharmacologically interesting, constituting the aim of this work.

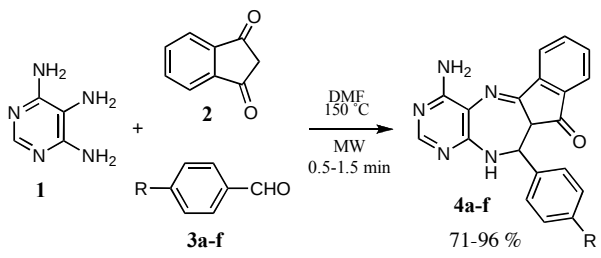
Another important feature consists in the application of microwave irradiation technology which has become a powerful synthetic tool in the efficient preparation of a wide range of organic compounds [19-21]. Microwave-assisted reaction methods simplify the synthetic processes and provide the possibility of working without solvent and under mild reaction conditions, giving rise to cleaner products with higher reaction rates [22-27].

In the present paper, we report the synthesis of new 11-amino-6-aryl-6,7-dihydroindeno[1,2-*e*]pyrimido[4,5-*b*]-[1,4]-diazepin-5(5a*H*)-ones **4a-f** and 9,11-diamino-6-aryl-6,7-dihydroindeno[1,2-*e*]pyrimido[4,5-*b*][1,4]diazepin-5(5a*H*)-ones **7a-f**. From the last series, the regioisomers 8,10-diamino-6-aryl-6,7-dihydroindeno[1,2-*e*]pyrimido-[5,4-*b*]-[1,4]diazepin-5(5a*H*)-ones **8a-c** were isolated in lower yields. All compounds were obtained as a racemic mixture employing microwave-assisted reaction techniques.

RESULTS AND DISCUSSION

The first series of derivatives was prepared by a single-step tricomponent process involving the microwave irradiation of an equimolar mixture 4,5,6-triamino-pyrimidine **1**, 1,3-indandione **2** and the proper aromatic aldehydes **3a-f**, in the presence of catalytic amounts of DMF as homogenizing media to afford the products **4a-f**, regioselectively desired, in good yield and with short irradiation times (see Scheme 1).

Scheme 1



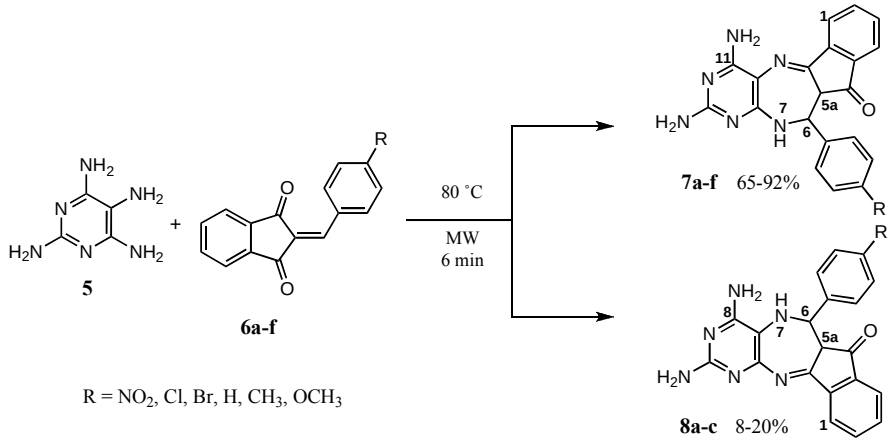
One-step tricomponent synthesis of derivatives **4a-f**.

The second series of compounds was synthesized by means of a bicomponent process instead of the previously described tricomponent approach, because 2,4,5,6-tetraaminopyrimidine **5** used as the starting material, reacts preferentially with benzaldehyde trough the amino group on C-5, giving rise to formation of undesired Schiff bases. The major nucleophilicity of such amino group compared to triamino analogue **1**, could be explained as a result of the electronic effect of the pyrimidine ring enhanced by the extra amino group on C-2 [28,29]. Given all this, the bicomponent approach was performed by subjecting to microwave irradiation, an equimolar and solvent-free mixture of 2,4,5,6-tetraaminopyrimidine **5** and the corresponding 2-arylideneindandiones **6a-f**, to afford derivatives **7a-f** in good yields, and the regioisomeric compounds **8a-c** in lower yield (see Scheme 2).

Structure elucidation of compounds **4a-f**, **7a-f** and **8a-c** was based on the spectral data (^{1}H NMR, ^{13}C NMR and mass spectrometry) summarized in the experimental section. In the ^{1}H NMR spectra for all compounds, two protons on the stereogenic centers (C-5a and C-6) of the 1,4-diazepine ring form an AX spin system. Proton H-5a appear as a doublet at δ = 3.94-4.24 ppm with a coupling constant of ^3J = 3.11-4.02 Hz, while proton H-6 (coupled with protons H-5a and diazepine NH) is usually observed at δ = 5.25-5.52 ppm (a doublet of doublets for all compounds) with $^3J_{\text{H-H}}$ = 3.11-4.02 Hz and $^3J_{\text{H-NH}}$ = 5.89-8.00 Hz. Analysis of the two dimensional NOESY experiment, confirmed the presence of the regioisomeric structures by showing a clear spatial correlation between NH_2 of the pyrimidine ring and NH of the 1,4-diazepine ring for compounds **8a-c**.

Finally, ^{13}C NMR, DEPT-135 and two dimensional heteronuclear NMR spectra provided the final structural

Scheme 2



Bicomponent synthesis of derivatives **7a-f** and **8a-c**.

The existence of non-equivalent amino groups at the *ortho*-position of tetraaminopyrimidine **5** has been reported previously [30,31], being the one on C-5 (as discussed above) the most nucleophilic. For this reason, the formation of regioisomers during the cyclization was expected due to the competition between nucleophilic addition of such amino group to the C=O and the Michael addition of the same nucleophile to the C=C double bond. We found that nucleophilic addition products **7a-f** were preferred to the Michael addition ones **8a-c**, obtained only with 2-arylideneindandiones **6a-c** (R = NO_2, Cl, Br) with the major electrophilicity at the β-carbon.

IR spectra for all compounds show typical bands between 3072 and 3450 cm^{-1} (NH and NH_2 groups) and 1538-1724 cm^{-1} (C=O, C=N and C=C groups). Nitro-derivatives (**4a**, **7a** and **8a**) show characteristic bands at 1344-1349 and 1515-1525 cm^{-1} due to NO_2 asymmetric and symmetric stretching vibrations, respectively.

elucidation of derivatives **4a-f**, **7a-f** and **8a-c**. Mass spectra of all compounds exhibit well defined molecular ions with particular fragmentation patterns involving the loss of CO ($M^{+\cdot}$-28) and Ar-C≡N. The latter fragmentation occurs by scission on C-C bond in *β* position to diazepine NH (type-B homolytic process) followed by a C-N cleavage (type-A_5 heterolytic process), which generates a constant and stable radical with high relative intensity [32].

In conclusion, we have achieved an efficient and practical one-step tricomponent synthesis of new 11-amino-6-aryl-6,7-dihydroindeno[1,2-*e*]pyrimido[4,5-*b*]-[1,4]diazepin-5(5a*H*)-ones **4a-f** and a versatile bi-component methodology for the preparation of 9,11-diamino-6-aryl-6,7-dihydroindeno[1,2-*e*]pyrimido[4,5-*b*]-[1,4]diazepin-5(5a*H*)-ones **7a-f** and the regioisomers 8,10-diamino-6-aryl-6,7-dihydroindeno[1,2-*e*]pyrimido-[5,4-*b*]-[1,4]diazepin-5(5a*H*)-ones **8a-c**. Interestingly, the

tricomponent synthesis leads to the regioselective formation of the desired product whereas the bicomponent approach proceeds with formation of the expected products and three additional regioisomers promoted by 2-arylideneindandiones **6a-c** with the major electrophilicity at the β-carbon. The remarkable features of the procedures developed and described herein are high conversion, shorter reaction times and solvent-free conditions.

EXPERIMENTAL

Melting points were determined in a Buchi Melting Point Apparatus and are uncorrected. The ^{1}H and ^{13}C NMR spectra were run on a Bruker DPX 400 spectrometer operating at 400 and 100 MHz, respectively, using dimethyl sulfoxide-d_6 as solvent and tetramethylsilane as internal standard. Mass spectra were obtained on a Hewlett Packard HP Engine- 5989 spectrometer (equipped with a direct inlet probe) operating at 70 eV. Elemental analyses have been obtained using a LECO CHNS-900 elemental analyzer. Reactions under microwave irradiation were performed using the CEM Discover LabMate® monomode system equipped with the IntelliVent™ Pressure Control Device, in open vessels under magnetic stirring and with maximum power of 300 W.

General procedure for synthesis of 11-amino-6-aryl-6,7-dihydroindeno[1,2-*e*]pyrimido[4,5-*b*][1,4]diazepin-5(5a*H*)-ones (4a-f). A mixture of dihydrochloride of triamine **1** (1.53 mmol), 1,3-indandione **2** (1.53 mmol) and *p*-substituted benzaldehydes **3a-f** with 0.2 mL of dry dimethylformamide, was subjected to microwave irradiation in open vessels under magnetic stirring for 0.5-1.5 min at 150 ºC and with a maximum power of 300 W. Reaction progress was controlled by TLC. After completion of the reaction, the resulting mixture was cooled down and treated by addition of dry ethanol (5 mL) under stirring, affording a precipitate which was collected by filtration and washed with water followed by cold ethanol to yield compounds **4a-f**.

11-Amino-6-(4-nitrophenyl)-6,7-dihydroindeno[1,2-*e*]pyrimido[4,5-*b*][1,4]diazepin-5(5a*H*)-one (4a). Orange powder (96%); mp 233 ºC (d); FTIR (KBr) ν 3360, 3223, 3073 (NH and NH_2); 1724 (C=O); 1643, 1593 (C=N and C=C); 1515, 1344 (NO_2) cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 4.24 (d, *J* = 3.72 Hz, 1H), 5.52 (dd, *J* = 3.52 Hz, *J* = 6.41 Hz, 1H), 7.15 (d, *J* = 8.90 Hz, 2H), 7.39 (s, 2H, NH_2), 7.58 (t, *J* = 7.86 Hz, 1H), 7.67 (d, *J* = 7.45 Hz, 1H), 7.75 (t, *J* = 7.86 Hz, 1H), 7.99 (d, *J* = 7.89 Hz, 2H), 8.21 (s, 1H), 8.38 (d, *J* = 7.86 Hz, 1H), 9.32 (d, *J* = 6.40 Hz, 1H, NH) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ 56.6, 56.8, 105.7, 122.9, 123.2, 123.5, 127.7, 132.4, 136.0, 137.9, 146.9, 147.1, 147.3, 149.0, 153.1, 157.8, 159.4, 197.4 ppm; Mass (*m/z*, %): 386 (M$^+$, 100), 358 (17), 264 (23), 250 (29), 236 (36). *Anal.* Calcd. For $C_{20}H_{14}N_6O_3$: C, 62.17; H, 3.65; N, 21.75. Found: C, 62.29; H, 3.61; N, 21.52.

11-Amino-6-(4-chlorophenyl)-6,7-dihydroindeno[1,2-*e*]pyrimido[4,5-*b*][1,4]diazepin-5(5a*H*)-one (4b). Pale yellow powder (82%); mp 217 ºC (d); FTIR (KBr) ν 3300, 3191, 3150 (NH and NH_2); 1723 (C=O); 1641, 1590, 1531 (C=N and C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 4.15 (d, *J* = 3.52 Hz, 1H), 5.40 (dd, *J* = 3.52 Hz, *J* = 6.41 Hz, 1H), 6.90 (d, *J* = 8.48 Hz, 2H), 7.21 (d, *J* = 8.48 Hz, 2H), 7.61 (t, *J* = 7.13 Hz, 1H), 7.69 (d, *J* = 7.65 Hz, 1H), 7.78 (t, *J* = 7.03 Hz, 1H), 8.23 (s, 1H), 8.32 (s, 2H, NH_2), 8.40 (d, *J* = 7.86 Hz, 1H), 9.38 (d, *J* = 6.41 Hz, 1H, NH) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ 56.6, 56.9, 105.2, 122.9, 123.2, 128.1, 128.4, 132.5, 132.6, 136.0, 138.1, 139.0, 147.0, 147.3, 152.9, 156.5, 160.3, 197.5 ppm; Mass (*m/z*, %): 375 (M$^+$, 100), 347 (24), 264 (29), 250 (36), 236 (89). *Anal.* Calcd. For $C_{20}H_{14}ClN_5O$: C, 63.92; H, 3.75; N, 18.64. Found: C, 63.78; H, 3.78; N, 18.77.

11-Amino-6-(4-bromophenyl)-6,7-dihydroindeno[1,2-*e*]pyrimido[4,5-*b*][1,4]diazepin-5(5a*H*)-one (4c). Yellow powder (89%); mp 224 ºC (d); FTIR (KBr) ν 3314, 3198, 3100 (NH and NH_2); 1715 (C=O); 1589 (C=N and C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 4.14 (d, *J* = 3.51 Hz, 1H), 5.37 (dd, *J* = 3.51 Hz, *J* = 6.41 Hz, 1H), 6.83 (d, *J* = 8.47 Hz, 2H), 7.35 (d, *J* = 8.47 Hz, 2H), 7.61 (t, *J* = 7.03 Hz, 1H), 7.68 (d, *J* = 7.65 Hz, 1H), 7.78 (t, *J* = 7.86 Hz, 1H), 8.21 (s, 1H), 8.36 (s, 2H, NH_2), 8.42 (d, *J* = 7.86 Hz, 1H), 9.33 (d, *J* = 6.41 Hz, 1H, NH) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ 56.6, 56.9, 105.3, 123.0, 128.5, 131.3, 132.5, 132.8, 136.0, 138.1, 139.5, 147.1, 147.8, 153.0, 156.8, 160.1, 197.6 ppm; Mass (*m/z*, %): 419 (M$^+$, 88), 391 (18), 264 (39), 250 (44), 236 (100). *Anal.* Calcd. For $C_{20}H_{14}BrN_5O$: C, 57.16; H, 3.36; N, 16.66. Found: C, 57.13; H, 3.48; N, 16.55.

11-Amino-6-phenyl-6,7-dihydroindeno[1,2-*e*]pyrimido[4,5-*b*][1,4]diazepin-5(5a*H*)-one (4d). Beige powder (82%); mp 234 ºC (d); FTIR (KBr) ν 3279, 3210, 3096 (NH and NH_2); 1723 (C=O); 1638, 1550 (C=N and C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 4.15 (d, *J* = 3.51 Hz, 1H), 5.40 (dd, *J* = 3.51 Hz, *J* = 6.41 Hz, 1H), 6.88-7.13 (m, 5H, Ph), 7.59 (t, *J* = 7.44 Hz, 1H), 7.69 (d, *J* = 7.65 Hz, 1H), 7.76 (t, *J* = 7.55 Hz, 1H), 8.27 (s, 1H), 8.39 (d, *J* = 7.85 Hz, 1H), 8.47 (s, 2H, NH_2), 9.54 (d, *J* = 6.41 Hz, 1H, NH) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ 57.0, 57.2, 105.0, 122.9, 123.2, 126.2, 128.0, 128.3, 132.5, 135.8, 138.2, 139.0, 139.8, 146.1, 147.0, 160.9, 197.4 ppm; Mass (*m/z*, %): 341 (M$^+$, 100), 313 (24), 264 (23), 250 (17), 236 (56). *Anal.* Calcd. For $C_{20}H_{15}N_5O$: C, 70.37; H, 4.43; N, 20.52. Found: C, 70.21; H, 4.48; N, 20.46.

11-Amino-6-(4-methylphenyl)-6,7-dihydroindeno[1,2-*e*]pyrimido[4,5-*b*][1,4]diazepin-5(5a*H*)-one (4e). White-yellow powder (71%); mp 280-282 ºC (d); FTIR (KBr) ν 3321, 3190, 3137 (NH and NH_2); 1722 (C=O); 1640, 1533 (C=N and C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.08 (s, 3H, CH_3), 4.13 (d, *J* = 3.51 Hz, 1H), 5.35 (dd, *J* = 3.52 Hz, *J* = 6.41 Hz, 1H), 6.77 (d, *J* = 8.27 Hz, 2H), 6.93 (d, *J* = 8.06 Hz, 2H), 7.60 (t, *J* = 7.44 Hz, 1H), 7.68 (d, *J* = 7.65 Hz, 1H), 7.77 (t, *J* = 7.54 Hz, 1H), 8.27 (s, 1H), 8.41 (d, *J* = 7.66 Hz, 1H), 8.46 (s, 2H, NH_2), 9.54 (d, *J* = 6.62 Hz, 1H, NH) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ 20.4, 56.8, 57.1, 104.9, 122.9, 123.2, 126.1, 128.9, 132.4, 135.8, 136.9, 137.2, 138.2, 146.1, 147.1, 152.8, 155.7, 160.9, 197.4 ppm; Mass (*m/z*, %): 355 (M$^+$, 100), 326 (30), 264 (15), 250 (15), 236 (67). *Anal.* Calcd. For $C_{21}H_{17}N_5O$: C, 70.97; H, 4.82; N, 19.71. Found: C, 70.81; H, 4.86; N, 19.53.

11-Amino-6-(4-methoxyphenyl)-6,7-dihydroindeno[1,2-*e*]-pyrimido[4,5-*b*][1,4]diazepin-5(5a*H*)-one (4f). Yellow powder (77%); mp 265-267 ºC (d); FTIR (KBr) ν 3430, 3218, 3072 (NH and NH_2); 1722 (C=O); 1640, 1568 (C=N and C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 3.56 (s, 3H, CH_3), 3.97 (d, *J* = 3.51 Hz, 1H), 5.26 (dd, *J* = 3.52 Hz, *J* = 6.41 Hz, 1H), 6.67 (d, *J* = 8.89 Hz, 2H), 6.79 (d, *J* = 8.68 Hz, 2H), 7.38 (s, 2H, NH_2), 7.55 (t, *J* = 7.03 Hz, 1H), 7.66 (d, *J* = 7.65 Hz, 1H), 7.73 (t, *J* = 7.65 Hz, 1H), 7.96 (s, 1H), 8.34 (d, *J* = 7.86 Hz, 1H), 8.59 (d, *J* = 6.41 Hz, 1H, NH) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ

54.8, 56.1, 57.3, 106.0, 113.5, 122.7, 122.8, 127.4, 131.7, 133.1, 135.7, 138.0, 147.7, 152.4, 153.6, 158.4, 158.5, 160.3, 198.2 ppm; Mass (*m/z*, %): 371 (M^{+}, 100), 342 (19), 328 (22), 264 (13), 250 (5), 236 (81). *Anal.* Calcd. For $C_{21}H_{17}N_5O_2$: C, 67.91; H, 4.61; N, 18.86. Found: C, 67.83; H, 4.67; N, 18.77.

General procedure for synthesis of 9,11-diamino-6-aryl-6,7-dihydroindeno[1,2-*e*]pyrimido[4,5-*b*][1,4]diazepin-5(5a*H*)-ones (7a-f) and 8,10-diamino-6-aryl-6,7-dihydroindeno[1,2-*e*]pyrimido[5,4-*b*][1,4]diazepin-5(5a*H*)-ones (8a-c). A dry mixture of tetraamine **5** (1.53 mmol) and 2-arylidene-indandiones **6a-f** (1.53 mmol) was subjected to microwave irradiation in open vessels at 80 °C with a maximum power of 300 W. The standard reaction time was estimated in 6 min by TLC control. After cooling, the resulting mixture was triturated with ethanol and the formed precipitate was collected by filtration and purified by silica gel chromatography with methylene chloride:methanol (20:1) as eluent to afford compounds **7a-c** in good yield and the regioisomers **8a-c** in lower yield. When the reaction was performed with arylidene derivatives **6d-f**, the resulting mixture was treated by addition of dry ethanol under stirring, affording a precipitate which was collected by filtration and washed with ethanol followed by hexane to yield compounds **7d-f** as single products.

9,11-Diamino-6-(4-nitrophenyl)-6,7-dihydroindeno[1,2-*e*]-pyrimido[4,5-*b*][1,4]diazepin-5(5a*H*)-one (7a). Orange powder (71%); mp 300-302 ºC (d); FTIR (KBr) ν 3444, 3389, 3188 (NH and NH_2); 1717 (C=O); 1664 (C=N and C=C); 1518, 1349 (NO_2) cm^{-1} ; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 3.95 (d, *J* = 4.00 Hz, 1H), 5.33 (dd, *J* = 4.02, *J* = 6.36, 1H), 6.02 (d, *J* = 8.00 Hz, 2H) , 7.14 (d, *J* = 8.00 Hz, 2H), 7.42 (t, *J* = 7.93 Hz, 1H), 7.44 (s, 2H, NH_2), 7.60 (d, *J* = 7.65 Hz, 1H), 7.66 (t, *J* = 7.93 Hz, 1H), 8.02 (s, 2H, NH_2), 8.18 (d, *J* = 7.65 Hz, 1H), 8.73 (d, *J* = 6.35 Hz, 1H, NH) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ 55.5, 56.7, 101.7, 122.0, 122.7, 123.4, 127.5, 130.3, 135.8, 136.8, 146.7, 148.6, 148.9, 151.1, 155.2, 163.7, 167.0, 198.8 ppm; Mass (*m/z*, %): 401 (M^{+}, 20), 373 (2), 372 (4), 279 (7), 251 (58). *Anal.* Calcd. For $C_{20}H_{15}N_7O_3$: C, 59.85; H, 3.77; N, 24.03. Found: C, 59.78; H, 3.69; N, 23.92.

9,11-Diamino-6-(4-chlorophenyl)-6,7-dihydroindeno[1,2-*e*]-pyrimido[4,5-*b*][1,4]diazepin-5(5a*H*)-one (7b). Yellow powder (92%); mp 305-307 ºC (d); FTIR (KBr) ν 3443, 3260, 3170 (NH and NH_2); 1719 (C=O); 1665 (C=N and C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 4.07 (d, *J* = 3.71 Hz, 1H), 5.33 (dd, *J* = 3.72 Hz, *J* = 6.21 Hz,1H), 6.91 (d, *J* = 8.69 Hz, 2H) , 7.22 (d, *J* = 8.69 Hz, 2H), 7.54 (t, *J* = 7.85 Hz, 1H), 7.60 (s, 2H, NH_2), 7.65 (d, *J* = 7.65 Hz, 1H), 7.73 (t, *J* = 7.85 Hz, 1H), 8.12 (s, 2H, NH_2), 8.36 (d, *J* = 7.65 Hz, 1H), 8.84 (d, *J* = 6.20 Hz, 1H, NH) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ 55.7, 56.5, 99.5, 122.8, 127.9, 128.1, 128.3, 131.5, 132.4, 135.8, 137.4, 139.1, 147.7, 151.6, 155.0, 198.0 ppm; Mass (*m/z*, %): 390 (M^{+}, 42), 362 (14), 361 (22), 279 (29), 251 (78). *Anal.* Calcd. For $C_{20}H_{15}ClN_6O$: C, 61.46; H, 3.87; N, 21.50. Found: C, 61.58; H, 3.79; N, 21.61.

9,11-Diamino-6-(4-bromophenyl)-6,7-dihydroindeno[1,2-*e*]-pyrimido[4,5-*b*][1,4]diazepin-5(5a*H*)-one (7c). Orange powder (89%); mp 310-312 ºC (d); FTIR (KBr) ν 3450, 3297, 3161 (NH and NH_2); 1719 (C=O); 1665 (C=N and C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 4.06 (d, *J* = 3.51 Hz, 1H), 5.30 (dd, *J* = 3.52, *J* = 6.41 Hz, 1H), 7.11 (d, *J* = 9.10 Hz, 2H) , 7.36 (d, *J* = 9.13 Hz, 2H), 7.54 (t, *J* = 7.03 Hz, 1H), 7.58 (s, 2H, NH_2), 7.66 (d, *J* = 7.65 Hz, 1H), 7.73 (t, *J* = 7.00 Hz, 1H), 8.10 (s, 2H, NH_2), 8.36 (d, *J* = 7.65 Hz, 1H), 8.83 (d, *J* = 6.41 Hz, 1H, NH) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ 55.7, 56.5, 99.5, 121.0, 122.8, 128.4, 131.2, 131.4, 135.8, 137.4, 139.5, 147.7, 151.7, 154.9, 158.0, 162.3, 198.0 ppm; Mass (*m/z*, %): 434 (M^{+}, 83), 408 (9), 407 (14), 279 (43), 251 (100). *Anal.* Calcd. For $C_{20}H_{15}BrN_6O$: C, 55.19; H, 3.47; N, 19.31. Found: C, 55.23; H, 3.59; N, 19.27.

9,11-Diamino-6-phenyl-6,7-dihydroindeno[1,2-*e*]pyrimido-[4,5-*b*][1,4]diazepin-5(5a*H*)-one (7d). Beige powder (65%); mp 309-311 ºC (d); FTIR (KBr) ν 3442, 3303, 3158 (NH and NH_2); 1715 (C=O); 1665 (C=N and C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 3.95 (d, *J* = 3.60, 1H), 5.40 (dd, *J* = 3.62, *J* = 6.43, 1H), 7.08 (d, *J* = 8.14 Hz, 2H) , 7.11-7.13 (m, 3H), 7.51 (t, *J* = 7.84 Hz, 1H), 7.54 (s, 2H, NH_2), 7.61 (d, *J* = 7.65 Hz, 1H), 7.62 (t, *J* = 7.84 Hz, 1H), 7.70 (s, 2H, NH_2), 8.29 (d, *J* = 7.65 Hz 1H), 8.71 (d, *J* = 6.45, 1H, NH) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ 55.4, 56.0, 119.6, 120.5, 122.6, 123.6, 126.6, 127.8, 128.3, 128.5, 131.0, 133.5, 134.1, 136.2, 144.9, 162.2, 191.9 ppm; Mass (*m/z*, %): 356 (M^{+}, 100), 328 (10), 327 (19), 279 (4), 251 (3). *Anal.* Calcd. For $C_{20}H_{16}N_6O$: C, 67.40; H, 4.53; N, 23.58. Found: C, 67.33; H, 4.57; N, 23.65.

9,11-Diamino-6-(4-methylphenyl)-6,7-dihydroindeno[1,2-*e*]-pyrimido[4,5-*b*][1,4]diazepin-5(5a*H*)-one (7e). Beige powder (84%); mp 272-274 ºC; FTIR (KBr) ν 3443, 3347, 3166 (NH and NH_2); 1718 (C=O); 1660 (C=N and C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.09 (s, 3H), 4.01 (d, *J* = 3.51 Hz, 1H), 5.28 (dd, *J* = 3.51 Hz, *J* = 6.34 Hz, 1H), 6.78 (d, *J* = 8.06 Hz, 2H) , 6.93 (d, *J* = 8.06 Hz, 2H), 7.52 (t, *J* = 7.03 Hz, 1H), 7.54 (s, 2H, NH_2), 7.61 (d, *J* = 7.65 Hz, 1H), 7.62 (t, *J* = 7.04 Hz, 1H), 7.70 (s, 2H, NH_2), 8.29 (d, *J* = 7.65 Hz, 1H), 8.71 (d, *J* = 6.32 Hz, 1H, NH) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ 55.9, 56.7, 99.4, 122.7, 126.1, 128.8, 131.3, 135.7, 136.9, 137.2, 137.5, 147.8, 151.4, 155.3, 198.1 ppm; Mass (*m/z*, %): 370 (M^{+}, 100), 342 (12), 341 (23), 280 (4), 251 (6). *Anal.* Calcd. For $C_{21}H_{18}N_6O$: C, 68.09; H, 4.90; N, 22.69. Found: C, 67.98; H, 4.98; N, 22.73.

9,11-Diamino-6-(4-methoxyphenyl)-6,7-dihydroindeno[1,2-*e*]pyrimido[4,5-*b*][1,4]diazepin-5(5a*H*)-one (7f). Beige powder (80%); mp 332-333ºC (d); FTIR (KBr) ν 3432, 3273, 3172 (NH and NH_2); 1719 (C=O); 1663 (C=N and C=C) cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 3.67 (s, 3H), 3.90 (d, *J* = 3.11 Hz, 1H), 5.34 (dd, *J* = 3.11, *J* = 6.21, 1H), 6.66 (d, *J* = 8.47 Hz, 2H) , 6.86 (d, *J* = 8.47 Hz, 2H), 7.52 (t, *J* = 7.24 Hz, 1H), 7.63 (s, 2H, NH_2), 7.65 (d, *J* = 7.65 Hz, 1H), 7.70 (t, *J* = 7.26 Hz, 1H), 7.98 (s, 2H, NH_2), 8.22 (d, *J* = 7.65 Hz, 1H), 8.51 (d, *J* = 6.20, 1H, NH) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ 55.5, 56.3, 113.2, 121.7, 122.0, 126.9, 130.6, 131.6, 134.8, 137.2, 151.9, 155.2, 158.3, 196.9 ppm; Mass (*m/z*, %): 386 (M^{+}, 100), 358 (10), 357 (19), 279 (18), 251 (87). *Anal.* Calcd. For $C_{21}H_{18}N_6O_2$: C, 65.27; H, 4.70; N, 21.75. Found: C, 65.33; H, 4.63; N, 21.73.

8,10-Diamino-6-(4-nitrophenyl)-6,7-dihydroindeno[1,2-*e*]-pyrimido[5,4-*b*][1,4]diazepin-5(5a*H*)-one (8a). Orange powder (8 %); mp 231-233 ºC (d); FTIR (KBr) ν 3442, 3332, 3189 (NH and NH_2); 1724 (C=O); 1661 (C=N and C=C); 1525, 1346 (NO_2) cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 4.09 (d, *J* = 3.52 Hz,1H), 5.41 (dd, *J* = 3.52 Hz, *J* = 8.00 Hz, 1H), 6.94 (s, 2H, NH_2) , 7.48 (d, *J* = 8.89 Hz, 2H), 7.52 (t, *J* = 7.85 Hz, 1H), 7.64 (s, 2H, NH_2), 7.71 (t, *J* = 7.85 Hz, 1H), 8.02 (d, *J* = 8.89 Hz, 2H), 8.28 (d, *J* = 9.10 Hz, 1H), 8.28 (d, *J* = 8.00 Hz, 1H, NH), 8.37 (d, *J* = 9.09 Hz, 1H) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ 55.8, 56.5, 122.5, 123.5, 124.3, 126.4, 127.6, 131.1, 135.9, 137.1, 146.8, 147.8 ppm; Mass (*m/z*, %): 401 (M^{+}, 20), 373 (2), 372 (4), 279 (7), 251 (58). *Anal.* Calcd. For $C_{20}H_{15}N_7O_3$: C, 59.85; H, 3.77; N, 24.03. Found: C, 59.92; H, 3.81; N, 24.10.

8,10-Diamino-6-(4-chlorophenyl)-6,7-dihydroindeno[1,2-*e*]-pyrimido[5,4-*b*][1,4]diazepin-5(5a*H*)-one (8b). Yellow powder (20 %); mp 280-283 ºC (d); FTIR (KBr) ν 3448, 3408, 3175 (NH and NH_2); 1714 (C=O); 1665 (C=N and C=C) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 3.94 (d, *J* = 3.31 Hz, 1H), 5.25 (dd, *J* = 3.31 Hz, *J* = 6.21 Hz, 1H), 6.70 (s, 2H, NH_2) , 6.88 (d, *J* = 8.27 Hz, 2H), 7.19 (d, *J* = 8.27 Hz, 2H), 7.35 (s, 2H, NH_2), 7.48 (t, *J* = 7.44 Hz, 1H), 7.62 (d, *J* = 7.86 Hz, 1H), 7.63 (t, *J* = 7.45 Hz, 1H), 8.13 (d, *J* = 6.20 Hz, 1H, NH), 8.25 (d, *J* = 7.86 Hz, 1H) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ 55.5, 56.7, 100.6, 122.3, 122.7, 128.1, 128.2, 130.8, 132.1, 135.7, 137.1, 139.9, 140.1, 148.2, 152.6, 198.4, 198.5 ppm; Mass (*m/z*, %): 390 (M^+, 42), 362 (14), 361 (22), 279 (29), 251 (78). *Anal.* Calcd. For $C_{20}H_{15}ClN_6O$: C, 61.46; H, 3.87; N, 21.50. Found: C, 61.39; H, 3.81; N, 21.47.

8,10-Diamino-6-(4-bromophenyl)-6,7-dihydroindeno[1,2-*e*]-pyrimido[5,4-*b*][1,4]diazepin-5(5a*H*)-one (8c). Orange powder (17 %); mp 272-274 ºC (d); FTIR (KBr) ν 3437, 3262, 3167 (NH and NH_2); 1719 (C=O); 1665 (C=N and C=C) cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz): δ 4.02 (d, *J* = 3.34 Hz, 1H), 5.34 (dd, *J* = 3.34 Hz, *J* = 5.89 Hz, 1H), 6.90 (s, 2H, NH_2) , 6.93 (d, *J* = 8.23 Hz, 2H), 7.25 (d, *J* = 8.23 Hz, 2H), 7.38 (s, 2H, NH_2), 7.51 (t, *J* = 7.42 Hz, 1H), 7.62 (d, *J* = 7.85 Hz, 1H), 7.68 (t, *J* = 7.42 Hz, 1H), 8.13 (d, *J* = 5.89 Hz, 1H, NH), 8.77 (d, *J* = 7.85 Hz, 1H) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): δ 53.4, 54.2, 101.4, 121.9, 122.3, 127.8, 128.0, 129.8, 132.0, 134.5, 135.2, 138.9, 140.3, 147.9, 150.3, 198.2, 198.5 ppm; Mass (*m/z*, %): 434 (M^+, 83), 408 (9), 407 (14), 279 (43), 251 (100). *Anal.* Calcd. For $C_{20}H_{15}BrN_6O$: C, 55.19; H, 3.47; N, 19.31. Found: C, 55.27; H, 3.40; N, 19.35.

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