An Efficient and Facile Synthesis of Pyrimidine and Quinazoline Derivatives via One-Pot Three-Component Reaction under Solvent-Free Conditions

Liangce Rong,* Hongxia Han, Haiying Wang, Hong Jiang, Shuajiang Tu, and Daqing Shi

Department of Chemistry, Xuzhou Normal University, Key Laboratory of Biotechnology for Medicinal Plant, Xuzhou, Jiangsu, 221116, People's Republic of China
*E-mail: lcrong2005@yahoo.com

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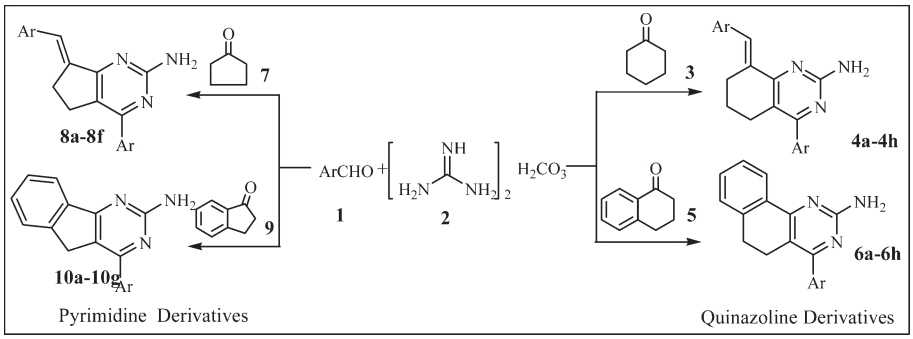

An efficient and convenient method for the preparation of pyrimidine and quinazoline derivatives by the one-pot reaction of aromatic aldehydes, cyclic ketones and guanidine carbonate, in the presence of sodium hydroxide under solvent-free condition was reported. This method has the advantages of excellent yields, mild reaction conditions, easy work-up, and being environmentally friendly over the existing procedures.

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INTRODUCTION

Pyrimidine and its derivatives, as the nitrogen-containing heterocycles, are extremely important compounds with high biological activities [1]. The quinazoline nucleus is also a very attractive and useful scaffold in medicinal chemistry: it can be found as a pharmacophore in a wide variety of biologically active compounds, such as antitumorals [2], antibacterials [3], antivirals [4], and many other therapeutic agents [5].

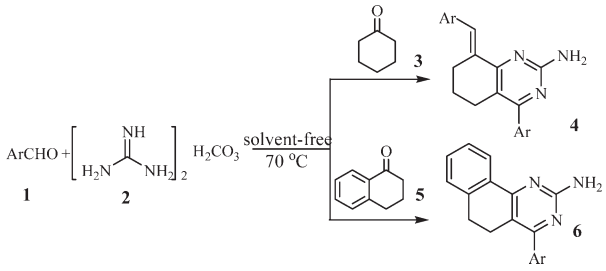
In recent years, because of increasing environmental concerns and the regulatory constraints faced in the chemical and pharmaceutical industries, the development of environmentally friendly organic synthesis has become a crucial and demanding area in modern organic chemical research [6]. In order to avoid using organic solvents, solvent-free organic reactions [7], a ''green'' organic chemistry method, have been of great interest. These have many advantages such as high efficiency and selectivity, easy separation and purification, mild reaction conditions, and reduction in waste produced. Many organic reactions have been carried out just by heating [8].

In continuation to our current studies on the application of solvent-free conditions for the synthesis of organic compounds [9], herein, we would like to report a practical and simple method to prepare pyrimidine and quinazoline derivatives by heating the starting materials under dry conditions.

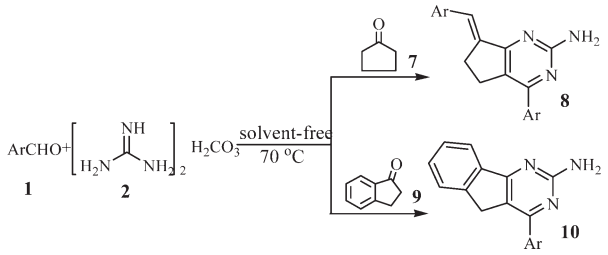
RESULTS AND DISCUSSION

At first, cyclohexanone (2 mmol), aromatic aldehyde (4 mmol), guanidine carbonate (1 mmol) and NaOH (0.2 g) were chosen to react together under solvent-free conditions at 70°C, and the reaction proceeded smoothly in short time (about 15 min) and the corresponding compounds 4-aryl-8-arylidene)-5,6,7,8-tetrahydroquinaz-olin-2-amine (**4a–4h**) could be gained with high yields (Scheme 1). Then, the reagent of 3,4-dihydronaphthalen-1(2*H*)-one (2 mmol) was chosen to replace cyclohexanone to react with aromatic aldehyde (2 mmol), guanidine carbonate (1 mmol) under the same conditions, and the corresponding fused-ring quinazoline derivatives: *viz*. 4-(4-bromophenyl)-5,6-dihydrobenzo[*h*]quinazolin-2-amine (**6a–6h**), were obgained with excellent yields. The results of reactions were listed in Table 1. As shown in Table 1, all the reactions proceeded smoothly with high yields. We also observed that electron-

Scheme 1



Scheme 2



withdrawing substituents (—Cl, —Br), and electron-donating substituents (—CH_3, —OCH_3) had no effect on the reaction.

In order to apply this reaction to a library synthesis, cyclopentanone and indan-1-one were chosen to react with aromatic aldehyde, and guanidine carbonate under same reaction conditions (Scheme 2). To our delight, all reactions could be completed successfully, and (*E*)-7-arylidene)-4-aryl-6,7-dihydro-5*H*-cyclopenta[*d*] pyrimidin-2-amine (**8a–8f**) and 4-aryl-5*H*-indeno[1,2-*d*]pyrimidin-2-amine (**10a–10g**) could be gained with good yields. The reaction results are summarized in Table 2. The structures of **4**, **6**, **8,** and **10** were confirmed by ir, ^{1}H NMR and elemental analysis, furthermore, the reported products were identified by comparison of melting point with those described in the literatures [10].

Although similar compounds have been reported in the literature and the disadvantages of reported methods were obvious, such as long reaction time, lower product yields and harsh conditions, furthermore, the excess of organic solvent was requisite.

In conclusion, an efficient method for the synthesis of pyrimidine and quinazoline derivatives by condensation of cyclic ketone, aromatic aldehydes, and guanidine carbonate was successfully established under solvent-free condition catalyzed by NaOH. The advantages of this procedure are high yields, mild reaction conditions, easy work-up, and environmentally friendly procedure.

Table 1

Synthesis of quinazoline derivatives under solvent-free conditions.

Entry	Ar[1]	Product	Yields
1	4-$CH_3C_6H_4$	**4a**	90
2	4-$CH_3OC_6H_4$	**4b**	95
3	3,4-$(CH_3)_2C_6H_3$	**4c**	96
4	3,4-$(CH_3O)_2C_6H_3$	**4d**	94
5	4-BrC_6H_4	**4e**	92
6	4-ClC_6H_4	**4f**	97
7	3-ClC_6H_4	**4g**	90
8	3,4-$Cl_2C_6H_3$	**4h**	95
9	4-$CH_3C_6H_4$	**6a**	96
10	4-$CH_3OC_6H_4$	**6b**	97
11	3,4-$(CH_3O)_2C_6H_3$	**6c**	96
12	4-FC_6H_4	**6d**	96
13	4-BrC_6H_4	**6e**	98
14	4-ClC_6H_4	**6f**	97
15	3,4-Cl_2C_6H	**6g**	93
16	C_6H_5	**6h**	95

EXPERIMENTAL

Melting points were determined on XT-5 microscopic melting-point apparatus and were uncorrected. IR spectra were recorded on a FT Bruker Tensor 27 spectrometer. ^{1}H NMR spectra were obtained from solution in DMSO-d_6 with Me_4Si as internal standard using a Bruker-400 spectrometer. Microanalyses were carried out using a Perkin-Elmer 2400 II analyzer.

General procedure for the synthesis of pyrimidine and quinazoline derivatives. The mixture of ketones **3** and **7**, or **5** and **9** (2 mmol), aromatic aldehydes **2** (4 mmol or 2 mmol), guanidine carbonate **3** (1 mmol) and NaOH (0.2 g) was put in a reaction flask and heated at 70°C for about 15 min. After completing the reaction, the reaction mixture was poured into water, and then washed with water thoroughly. The product was filtered, dried, and recrystallized from 95% ethanol.

(*E*)-8-(4-Methylbenzylidene)-4-*p*-tolyl-5,6,7,8-tetrahydroquinazolin-2-amine (4a). This compound was obtained as yellow crystals, mp 210–212°C, Lit. [10d] 210–212°C; ir (KBr, ν, cm^{-1}): 3502, 3282, 3152, 2929, 1626, 1541, 1456, 1220; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 8.00 (1H, s, ArCH=),

Table 2

Synthesis of pyrimidine derivatives under solvent-free conditions.

Entry	Ar[1]	Product	Yields
1	4-$CH_3C_6H_4$	**8a**	93
2	4-$CH_3OC_6H_4$	**8b**	92
3	4-FC_6H_4	**8c**	90
4	4--ClC_6H_4	**8d**	93
5	3-ClC_6H_4	**8e**	90
6	4-BrC_6H_4	**8f**	95
7	4-$CH_3C_6H_4$	**10a**	93
8	4-$CH_3OC_6H_4$	**10b**	92
9	3,4-$(CH_3O)_2C_6H_3$	**10c**	93
10	4-FC_6H_4	**10d**	90
11	4-ClC_6H_4	**10e**	93
12	4-BrC_6H_4	**10f**	90
13	3,4-$Cl_2C_6H_3$	**10g**	95

7.45 (2H, d, J = 7.2 Hz, ArH), 7.36 (2H, d, J = 8.0 Hz, ArH), 7.26 (4H, t, J = 8.8 Hz, ArH), 6.33 (2H, s, NH_2), 2.78 (2H, t, J = 5.2 Hz, CH_2), 2.60 (2H, t, J = 5.2 Hz, CH_2), 2.37 (3H, s, CH_3), 2.34 (3H, s, CH_3), 1.63 (2H, t, J = 5.2 Hz, CH_2). Anal. Calcd. For $C_{23}H_{23}N_3$: C 80.90, H 6.79, N 12.31. Found: C 80.72, H 6.73, N 12.25.

(*E*)-8-(4-Methoxybenzylidene)-4-(4-methoxyphenyl)-5,6,7,8-tetrahydroquinazolin-2-amine (4b). This compound was obtained as yellow crystals, mp 230–232°C, Lit. [10d] 245–247°C; ir (KBr, ν, cm^{-1}): 3482, 3377, 3202, 2934, 1606, 1579, 1538, 1509, 1447, 1406, 1356, 1333, 1298, 1247; ^{1}H NMR (400MHz, DMSO-d_6) (δ, ppm): 7.98 (1H, s, ArCH=), 7.53 (2H, d, J = 8.4 Hz, ArH), 7.42 (2H, d, J = 8.4 Hz, ArH), 7.01 (4H, dd, J = 6.0 Hz, J = 6.0 Hz, ArH), 6.28 (2H, s, NH_2), 3.81 (3H, s, OCH_3), 2.80 (3H, s, OCH_3), 2.79 (2H, t, J = 5.6 Hz, CH_2), 2.64 (2H, t, J = 5.6 Hz, CH_2), 1.62 (2H, t, J = 5.2 Hz, CH_2). Anal. Calcd. For $C_{23}H_{23}N_3O_2$: C 73.97, H 6.21, N 11.25. Found: C 73.78, H 6.27, N 11.31.

(*E*)-8-(3,4-Dimethylbenzylidene)-4-(3,4-dimethylphenyl)-5,6,7,8-tetrahydroquinazolin-2-amine (4c). This compound was obtained as yellow crystals, mp 191–193°C; ir (KBr, ν, cm^{-1}): 3494, 3284, 3155, 2921, 1625, 1540, 1503, 1459, 1359, 1335, 1221; 1H NMR (400MHz, DMSO-d_6) (δ, ppm): 7.98 (1H, s, ArCH=), 7.33 (1H, s, ArH), 7.25 (3H,m, ArH), 7.19 (2H, t, J = 8.8 Hz, ArH), 6.30 (2H, s, NH_2), 2.80 (2H, t, J = 5.2 Hz, CH_2), 2.61 (2H, t, J = 5.2 Hz, CH_2), 2.28 (6H, s, $2CH_3$), 2.27 (3H, s, CH_3), 2.25 (3H, s, CH_3),1.61 (2H, t, J = 5.2 Hz, CH_2). Anal. Calcd. For $C_{25}H_{27}N_3$: C 81.26, H 7.37, N 11.37. Found: C 81.51, H 7.35, N 11.40.

(*E*)-8-(3,4-Dimethoxybenzylidene)-4-(3,4-dimethoxyphenyl)-5,6,7,8-tetrahydroquinazolin-2-amine (4d). This compound was obtained as yellow crystals, mp 249–251°C, Lit. [10d] 231–233°C; ir (KBr, ν, cm^{-1}): 3484, 3280, 3154, 3074, 2936, 1619, 1541, 1459, 1260, 1234; ^{1}H NMR (400MHz, DMSO-d_6) (δ, ppm): 7.99 (1H, s, ArCH=), 7.11–7.15 (2H, m, ArH), 7.03 (4H, dd, J = 8.0 Hz, J = 8.0 Hz, ArH), 6.28 (2H, s, NH_2), 3.81 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 3.79 (3H, s, OCH_3), 3.77 (3H, s, OCH_3), 2.84 (2H, t, J = 5.2 Hz, CH_2), 2.65 (2H, t, J = 5.2 Hz, CH_2), 1.63 (2H, t, J = 5.2 Hz, CH_2). Anal. Calcd. For $C_{25}H_{27}N_3O_4$: C 69.27, H 6.28, N 9.69. Found: C 69.08, H 6.35, N 9.61.

(*E*)-8-(4-Bromobenzylidene)-4-(4-bromophenyl)-5,6,7,8-tetrahydroquinazolin-2-amine (4e). This compound was obtained as yellow crystals, mp 211–213°C; ir (KBr, ν, cm^{-1}): 3488, 3287, 3157, 2934, 1625, 1591, 1540, 1486, 1456, 1332, 1231; ^{1}H NMR (400MHz, DMSO-d_6) (δ, ppm): 7.98 (1H, s, ArCH=), 7.67 (2H, d, J = 8.4 Hz, ArH), 7.62 (2H, d, J = 8.4 Hz, ArH), 7.52 (2H, d, J = 8.4 Hz, ArH), 7.41 (2H, d, J = 8.4 Hz, ArH), 6.45 (2H, s, NH_2), 2.77 (2H, t, J = 5.2 Hz, CH_2), 2.60 (2H, t, J = 6.0 Hz, CH_2), 1.63 (2H, t, J = 5.2 Hz, CH_2). Anal. Calcd. For $C_{21}H_{17}Br_2N_3$: C 53.53, H 3.64, N 8.92. Found: C 53.33, H 3.62, N 8.96.

(*E*)-8-(4-Chlorobenzylidene)-4-(4-chlorophenyl)-5,6,7,8-tetrahydroquinazolin-2-amine (4f). This compound was obtained as yellow crystals, mp 195–197°C, Lit. [10d] 224–226°C; ir (KBr, ν, cm^{-1}): 3497, 3319, 3202, 2939, 1631, 1606, 1543, 1507, 1464, 1417, 1357, 1333, 1317, 1224; ^{1}H NMR (400MHz, DMSO-d_6) (δ, ppm): 8.01 (1H, s, ArCH=), 7.61 (2H, dd, J = 6.0 Hz, J = 6.0 Hz, ArH), 7.51 (2H, dd, J = 6.0 Hz, J = 6.0 Hz, ArH), 7.28 (4H, q, J = 8.8 Hz, J = 6.4 Hz, ArH), 6.41 (2H, s, NH_2), 2.78 (2H, br, CH_2), 2.60 (2H, t, J = 5.2 Hz, J = 5.2 Hz, CH_2), 1.63 (2H, t, J = 5.2 Hz, J = 5.2 Hz, CH_2). Anal. Calcd. For $C_{21}H_{17}Cl_2N_3$: C 65.98, H 4.48, N 10.99. Found: C 65.72, H 4.55, N 10.68.

(*E*)-8-(3-Chlorobenzylidene)-4-(3-chlorophenyl)-5,6,7,8-tetrahydroquinazolin-2-amine (4g). This compound was obtained as yellow crystals, mp 237–238°C; ir (KBr, ν, cm^{-1}): 3484, 3285, 3157, 3078, 2932, 1624, 1592, 1543, 1461, 1436, 1411, 1351, 1334, 1268, 1219; ^{1}H NMR (400MHz, DMSO-d_6) (δ, ppm): 7.98 (1H, s, ArCH=), 7.60 (1H, s, ArH), 7.38-7.54 (7H, m, ArH), 6.48 (2H, s, NH_2), 2.78 (2H, t, J = 5.2 Hz, CH_2), 2.61 (2H, t, J = 6.0 Hz, CH_2), 1.63 (2H, t, J = 5.2 Hz, CH_2). Anal. Calcd. For $C_{21}H_{17}Cl_2N_3$: C 65.98, H 4.48, N 10.99. Found: C 65.80, H 4.50, N 10.95.

(*E*)-8-(3,4-Dichlorobenzylidene)-4-(3,4-dichlorophenyl)-5,6,7,8-tetrahydroquinazolin-2-amine (4h). This compound was obtained as yellow crystals, mp 200–202°C; ir (KBr, ν, cm^{-1}): 3479, 3296, 3184, 1625, 1541, 1472, 1415, 1389, 1351, 1331, 1215; ^{1}H NMR (400MHz, DMSO-d_6) (δ, ppm): 7.95 (1H, s, ArCH=), 7.82 (1H, s, ArH), 7.74 (1H, J = 8.4 Hz, ArH), 7.68 (2H, J = 8.4 Hz, ArH), 7.57 (1H, J = 8.4 Hz, ArH), 7.44 (1H, J = 8.4 Hz, ArH) 6.53 (2H, s, NH_2), 2.77 (2H, t, J = 5.2 Hz, J = 5.2 Hz, CH_2), 2.61 (2H, t, J = 6.0 Hz, J = 6.0 Hz, CH_2), 1.63 (2H, t, J = 5.2 Hz, J = 5.2 Hz, CH_2). Anal. Calcd. For $C_{21}H_{15}Cl_4N_3$: C 55.90, H 3.35, N 9.31. Found: C 55.78, H 3.34, N 9.34.

4-*p*-Tolyl-5,6-dihydrobenzo[*h*]quinazolin-2-amine (6a). This compound was obtained as yellow crystals, mp 192–194°C, Lit. [10g] 193–194°C; ir (KBr, ν, cm^{-1}): 3472, 3394, 3296, 2940, 1613, 1586, 1545, 1445, 1373, 1322, 1210; ^{1}H NMR (400MHz, DMSO-d6) (δ, ppm): 8.18 (1H, dd, J = 1.2 Hz, J = 1.6 Hz, ArH), 7.48 (2H, d, J = 8.0 Hz, ArH), 7.39 (2H, q, J = 6.8 Hz, J = 7.2 Hz, ArH), 7.29 (3H, d, J = 7.6 Hz, ArH), 6.48 (2H, s, NH_2), 2.77 (4H, s, $2CH_2$), 2.38 (3H, s, CH_3). Anal. Calcd. For $C_{19}H_{17}N_3$: C 79.41, H 5.96, N 14.62. Found: C 79.60, H 5.89, N 14.70.

4-(4-Methoxyphenyl)-5,6-dihydrobenzo[*h*]quinazolin-2-amine (6b). This compound was obtained as yellow crystals, mp 186–187°C, Lit. [10g] 182–183°C; ir (KBr, ν, cm^{-1}): 3467, 3287, 3178, 2940, 2830, 1609, 1578, 1547, 1510, 1453, 1405, 1374, 1322, 1302, 1277, 1251, 1214; ^{1}H NMR (400MHz, DMSO-d_6) (δ, ppm): 8.18 (1H, dd, J = 1.2 Hz, J = 1.6 Hz, ArH), 7.56 (2H, d, J = 8.4 Hz, ArH), 7.39 (2H, q, J = 6.0 Hz, J = 7.2 Hz, ArH), 7.32 (1H, d, J = 6.0 Hz, ArH), 7.04 (2H, d, J = 8.4 Hz, ArH), 6.47 (2H, s, NH_2), 3.82 (3H, s, CH_3O), 2.78 (4H, d, J = 3.2 Hz, $2CH_2$). Anal. Calcd. For $C_{19}H_{17}N_3O$: C 75.23, H 5.65, N 13.85. Found: C 75.42, H 5.69, N 13.79.

4-(3,4-Dimethoxyphenyl)-5,6-dihydrobenzo[*h*]quinazolin-2-amine (6c). This compound was obtained as yellow crystals, mp 198–200°C, Lit. [10c] 203–204°C; ir (KBr, ν, cm^{-1}): 3437, 3341, 3221, 2996, 2957, 1625, 1603, 1583, 1543, 1511, 1451, 1420, 1388, 1370, 1329, 1209; ^{1}H NMR (400MHz, DMSO-d_6) (δ, ppm): 8.17 (1H, dd, J = 1.2 Hz, J = 1.6 Hz, ArH), 7.39 (2H, q, J = 6.4 Hz, J = 7.2 Hz, ArH), 7.29 (1H, d, J = 6.4 Hz, ArH), 7.18 (1H, s, ArH), 7.14 (1H, d, J = 8.0 Hz, ArH), 7.05 (1H, d, J = 8.0 Hz, ArH), 6.48 (2H, s, NH_2), 3.82 (3H, s, CH_3O), 3.79 (3H, s, CH_3O), 2.82 (2H, t, J = 1.6 Hz, J = 4.0 Hz, CH_2), 2.78 (2H, t, J = 1.6 Hz, J = 4.0 Hz, CH_2). Anal. Calcd. For $C_{20}H_{19}N_3O_2$: C 72.05, H 5.74, N 12.60. Found: C 72.21, H 5.69, N 12.71.

4-(4-Fluorophenyl)-5,6-dihydrobenzo[*h*]quinazolin-2-amine (6d). This compound was obtained as yellow crystals, mp 194–196°C; ir (KBr, ν, cm^{-1}): 3489, 3302, 3175, 2946, 1627, 1604, 1553, 1499, 1452, 1413, 1398, 1373, 1321, 1297, 1222; ^{1}H NMR (400MHz, DMSO-d_6) (δ, ppm): 8.18 (1H, dd, J = 1.2 Hz, J = 1.6 Hz, ArH), 7.64 (2H, dd, J = 5.6 Hz, J = 5.6 Hz, ArH), 7.40 (2H, q, J = 7.2 Hz, J = 8.0 Hz, ArH), 7.30 (3H, dd, J = 5.6 Hz, J = 8.0 Hz, ArH), 6.53 (2H, s, NH_2), 2.77 (4H, s, $2CH_2$). Anal. Calcd. For $C_{18}H_{14}FN_3$: C 74.21, H 4.84, N 14.42. Found: C 74.35, H 4.82, N 14.46.

4-(4-Bromophenyl)-5,6-dihydrobenzo[*h*]quinazolin-2-amine (6e). This compound was obtained as yellow crystals, mp 228–230°C; ir (KBr, ν, cm^{-1}): 3385, 3319, 3216, 2942, 1634, 1589, 1569, 1541, 1487, 1450, 1413, 1390, 1371, 1322, 1211; ^{1}H NMR (400MHz, DMSO-d_6) (δ, ppm): 8.18 (1H, dd, J = 1.2 Hz, J = 1.6 Hz, ArH), 7.69 (2H, d, J = 8.4 Hz, ArH), 7.55 (2H, d, J = 8.4 Hz, ArH), 7.40 (2H, q, J = 6.8 Hz, J = 8.4 Hz, ArH), 7.30 (1H, d, J = 6.8 Hz, ArH), 6.56 (2H, s, NH_2), 2.77 (4H, s, $2CH_2$). Anal. Calcd. For $C_{18}H_{14}BrN_3$: C 61.38, H 4.01, N 11.93. Found: C 61.50, H 4.03, N 11.90.

4-(4-Chlorophenyl)-5,6-dihydrobenzo[*h*]quinazolin-2-amine (6f). This compound was obtained as yellow crystals, mp 216–218°C, Lit. [10g] 222–223°C; ir (KBr, ν, cm^{-1}): 3391, 3327, 3221, 2942, 1638, 1597, 1586, 1572, 1543, 1492, 1458, 1412, 1394, 1372, 1323, 1212; ^{1}H NMR (400MHz, DMSO-d_6) (δ, ppm): 8.18 (1H, dd, J = 1.2 Hz, J = 1.6 Hz, ArH), 7.62 (2H, d, J = 8.4 Hz, ArH), 7.55 (2H, d, J = 8.4 Hz, ArH), 7.40 (2H, q, J = 6.0 Hz, J = 8.4 Hz, ArH), 7.30 (1H, d, J = 6.4 Hz, ArH), 6.56 (2H, s, NH_2), 2.77 (4H, s, $2CH_2$). Anal. Calcd. For $C_{18}H_{14}ClN_3$: C 70.24, H 4.58, N 13.65. Found: C 70.43, H 4.50, N 13.58.

4-(3,4-Dichlorophenyl)-5,6-dihydrobenzo[*h*]quinazolin-2-amine (6g). This compound was obtained as yellow crystals, mp 210–212°C, Lit. [10c] 221–223°C; ir (KBr, ν, cm^{-1}): 3485, 3297, 3183, 2934, 1622, 1564, 1544, 1492, 1470, 1450, 1410, 1386, 1365, 1350, 1317, 1298, 1247, 1212; ^{1}H NMR (400MHz, DMSO-d_6) (δ, ppm): 8.18 (1H, d, J = 7.2 Hz, ArH), 7.84 (1H, d, J = 2.0 Hz, ArH), 7.56 (1H, d, J = 8.4 Hz, ArH), 7.58 (1H, dd, J = 2.0 Hz, J = 2.0 Hz, ArH), 7.40 (2H, q, J = 7.2 Hz, J = 8.0 Hz, ArH), 7.30 (1H, d, J = 7.2 Hz, ArH), 6.63 (2H, s, NH_2), 2.78 (4H, s, CH_2). Anal. Calcd. For $C_{18}H_{13}Cl_2N_3$: C 63.17, H 3.83, N 12.28. Found: C 63.40, H 3.76, N 12.21.

4-Phenyl-5,6-dihydrobenzo[*h*]quinazolin-2-amine (6h). This compound was obtained as yellow crystals, mp 164–165°C, Lit. [10h] 174–175°C; ir (KBr, ν, cm^{-1}): 3387, 3321, 3214, 2936, 1634, 1606, 1585, 1544, 1495, 1451, 1440, 1411, 1373, 1384, 1322, 1208; ^{1}H NMR (400MHz, DMSO-d_6) (δ, ppm): 8.18 (1H, dd, J = 1.2 Hz, J = 1.6 Hz, ArH), 7.57 (2H, dd, J = 1.6 Hz, J = 2.0 Hz, ArH), 7.47-7.52 (3H, m, ArH), 7.40 (2H, q, J = 5.6 Hz, J = 7.6 Hz, ArH), 7.30 (1H, d, J = 7.6 Hz, ArH), 6.51 (2H, s, NH_2), 2.77 (4H, s, CH_2). Anal. Calcd. For $C_{18}H_{15}N_3$: C 79.10, H 5.53, N 15.37. Found: C 79.33, H 5.48, N 15.25.

(*E*)-7-(4-Methylbenzylidene)-4-p-tolyl-6,7-dihydro-5*H*-cyclopenta[*d*]pyrimidin-2-amine (8a). This compound was obtained as yellow crystals, mp 229–230°C; ir (KBr, ν, cm^{-1}): 3474, 3313, 3184, 2916, 1624, 1549, 1510, 1455, 1413, 1361, 1224, 1202; ^{1}H NMR (400MHz, DMSO-d_6) (δ, ppm): 7.84 (2H, d, J = 8.0 Hz, ArH), 7.45 (2H, d, J = 8.0 Hz, ArH), 7.41 (1H, s, ArCH=), 7.31 (2H, d, J = 8.0 Hz, ArH), 7.24 (2H, J = 8.0 Hz, ArH), 6.51 (2H, s, NH_2), 3.12 (2H, d, J = 7.2 Hz, CH_2), 3.04 (2H, d, J = 4.0 Hz, CH_2), 2.37 (3H, s, CH_3), 2.33 (3H, s, CH_3). Anal. Calcd. For $C_{22}H_{21}N_3$: C 80.70, H 6.46, N 12.83. Found: C 80.86, H 6.48, N 12.80.

(*E*)-7-(4-Methoxybenzylidene)-4-(4-methoxyphenyl)-6,7-dihydro-5*H*-cyclopenta[*d*]pyrimidin-2-amine (8b). This compound was obtained as yellow crystals, mp 256–258°C; ir (KBr, ν, cm^{-1}): 3475, 3370, 3217, 2934, 1624, 1606, 1582, 1542, 1510, 1460, 1440, 1399, 1366, 1308, 1248, 1220; ^{1}H NMR (400MHz, DMSO-d_6) (δ, ppm): 7.94 (2H, d, J = 8.8 Hz, ArH), 7.53 (2H, d, J = 8.8 Hz, ArH), 7.39 (1H, s, ArCH=), 7.07 (2H, d, J = 8.8 Hz, ArH), 7.02 (2H, d, J = 8.8 Hz, ArH), 6.42 (2H, s, NH_2), 3.83 (3H, s, CH_3O), 3.80 (3H, s, CH_3O), 3.17 (2H, t, J = 6.4 Hz, CH_2), 3.06 (2H, t, J = 6.4 Hz, CH_2). Anal. Calcd. For $C_{22}H_{21}N_3O_2$: C 73.52, H 5.89, N 11.69. Found: C 73.38, H 5.91, N 11.73.

(*E*)-7-(4-fluorobenzylidene)-4-(4-fluorophenyl)-6,7-dihydro-5*H*-cyclopenta[*d*]pyrimidin-2-amine (8c). This compound was obtained as yellow crystals, mp 187–189°C; ir (KBr, ν, cm^{-1}): 3485, 3337, 3239, 3064, 2934, 1624, 1615, 1582, 1542, 1509, 1459, 1440, 1316, 1248, 1227; ^{1}H NMR (400MHz, DMSO-d_6) (δ, ppm): 8.01(2H, dd, J = 5.6 Hz, J = 5.6 Hz, ArH), 7.63 (2H, dd, J = 5.6 Hz, J = 5.6 Hz, ArH), 7.43 (1H, s, ArCH=), 7.35 (2H, t, J = 8.8 Hz, ArH), 7.27 (2H, t, J = 8.8 Hz, ArH), 6.57 (2H, s, NH_2), 3.15 (2H, d, J = 7.2 Hz, CH_2), 3.08 (2H, t, J = 4.4 Hz, J = 4.4 Hz, CH_2). Anal. Calcd. For $C_{20}H_{15}F_2N_3$: C 71.63, H 4.51, N 12.53. Found: C 71.47, H 4.53, N 12.48.

(*E*)-7-(4-Chlorobenzylidene)-4-(4-chlorophenyl)-6,7-dihydro-5*H*-cyclopenta[*d*]pyrimidin-2-amine (8d). This compound was obtained as yellow crystals, mp 165–167°C; ir (KBr, ν, cm^{-1}): 3483, 3323, 3192, 2928, 1672, 1623, 1594, 1544, 1492, 1460, 1407, 1361, 1295, 1225; ^{1}H NMR (400MHz, DMSO-d_6) (δ, ppm): 7.97 (2H, d, J = 8.8 Hz, ArH), 7.62 (2H, d, J = 8.8 Hz, ArH), 7.58 (1H, s, ArCH=), 7.50 (2H, d, J = 8.8 Hz, ArH), 7.42 (2H, t, J = 8.8 Hz, ArH), 6.63 (2H, s, NH_2), 3.16 (2H, d, J = 6.8 Hz, CH_2), 3.09 (2H, t, J = 6.8 Hz, CH_2). Anal. Calcd. For $C_{20}H_{15}Cl_2N_3$: C 65.23, H 4.11, N 11.41. Found: C 65.48, H 4.13, N 11.37.

(*E*)-7-(3-Chlorobenzylidene)-4-(3-chlorophenyl)-6,7-dihydro-5*H*-cyclopenta[*d*]pyrimidin-2-amine (8e). This compound was obtained as yellow crystals, mp 135–137°C; ir (KBr, ν, cm^{-1}): 3469, 3298, 3174, 2913, 1689, 1621, 1590, 1561, 1541, 1476, 1459, 1421, 1351, 1279, 1250, 1228, 1205; ^{1}H NMR (400MHz, DMSO-d_6) (δ, ppm): 8.01 (2H, d, J = 7.6 Hz, ArH), 7.68 (2H, d, J = 6.8 Hz, ArH), 7.61 (1H, s, ArCH=), 7.54 (2H, d, J = 6.8 Hz, ArH), 7.40 (2H, d, J = 7.6 Hz, ArH), 6.67 (2H, s, NH_2), 3.18 (2H, t, J = 5.6 Hz, CH_2), 3.03 (2H, t, J = 5.6 Hz, CH_2). Anal. Calcd. For $C_{20}H_{15}Cl_2N_3$: C 65.23, H 4.11, N 11.41. Found: C 65.48, H 4.13, N 11.37.

(*E*)-7-(4-Bromobenzylidene)-4-(4-bromophenyl)-6,7-dihydro-5*H*-cyclopenta[*d*]pyrimidin-2-amine (8f). This compound was obtained as yellow crystals, mp 180–182°C; ir (KBr, ν, cm^{-1}): 3454, 3293, 3170, 2956, 1672, 1620, 1588, 1488, 1459, 1403, 1351, 1176; ^{1}H NMR (400MHz, DMSO-d_6) (δ, ppm): 7.95 (2H, d, J = 8.8 Hz, ArH), 7.70 (2H, d, J = 8.8 Hz, ArH), 7.66 (1H, s, ArCH=), 7.59 (2H, d, J = 8.8 Hz, ArH), 7.42 (2H, d, J = 8.8 Hz, ArH), 6.98 (2H, s, NH_2), 3.09 (2H, t, J = 5.6 Hz, CH_2), 2.88 (2H, t, J = 5.6 Hz, CH_2). Anal. Calcd. For $C_{20}H_{15}Br_2N_3$: C 52.54, H 3.31, N 9.19. Found: C 52.67, H 3.34, N 9.15.

4-*p*-Tolyl-5*H*-indeno[1,2-*d*]pyrimidin-2-amine (10a). This compound was obtained as yellow crystals, mp 199–200°C; ir (KBr, ν, cm^{-1}): 3480, 3305, 3177, 2898, 1625, 1586, 1561, 1509, 1483, 1465, 1452, 1413, 1398, 1369, 1308, 1251; ^1H NMR (400MHz, DMSO-d_6) (δ, ppm): 8.02 (2H, d, J = 8.0 Hz, ArH), 7.91 (1H, d, J = 7.6 Hz, ArH), 7.68 (1H, d, J = 7.2 Hz, ArH), 7.54 (1H, t, J = 7.2 Hz, ArH), 7.48 (1H, t, J = 7.2 Hz, ArH), 7.36 (2H, J = 8.0 Hz, ArH), 6.64 (2H, s, NH_2), 4.12 (2H, s, CH_2), 2.40 (3H, s, CH_3). Anal. Calcd. For $C_{18}H_{15}N_3$: C 79.10, H 5.53, N 15.37. Found: C 79.35, H 5.51, N 15.31.

4-(4-Methoxyphenyl)-5*H*-indeno[1,2-*d*]pyrimidin-2-amine (10b). This compound was obtained as yellow crystals, mp 206–208°C, Lit. [10f] 240–241°C; ir (KBr, ν, cm^{-1}): 3312, 3178, 2887, 1643, 1608, 1591, 1567, 1533, 1510, 1481, 1466, 1438, 1422, 1395, 1370, 1301, 1255, 1209; ^1H NMR (400MHz, DMSO-d_6) (δ, ppm): 8.11 (2H, d, J = 8.8 Hz, ArH), 7.94 (1H, d, J = 7.6 Hz, ArH), 7.68 (1H, d, J = 7.2 Hz, ArH), 7.54 (1H, t, J = 7.2 Hz, ArH), 7.48 (1H, t, J = 7.2 Hz, ArH), 7.11 (2H, J = 8.0 Hz, ArH), 6.60 (2H, s, NH_2), 4.12 (2H, s, CH_2), 3.85 (3H, s, CH_3O). Anal. Calcd. For $C_{18}H_{15}N_3O$: C 74.72, H 5.23, N 14.52. Found: C 74.58, H 5.30, N 14.61.

4-(3,4-Dimethoxyphenyl)-5*H*-indeno[1,2-*d*]pyrimidin-2-amine (10c). This compound was obtained as yellow crystals, mp 271–273°C; ir (KBr, ν, cm^{-1}): 3405, 3310, 3189, 2962, 2935, 1640, 1604, 1542, 1511, 1484, 1463, 1449, 1423, 1401, 1378, 1326, 1250, 1235, 1211; ^1H NMR (400MHz, DMSO-d_6) (δ, ppm): 7.91 (1H, d, J = 7.6 Hz, ArH), 7.68–7.72 (3H, m, ArH), 7.49–7.54 (2H, m, ArH), 7.12 (1H, d, J = 8.0 Hz, ArH), 6.60 (2H, s, NH_2), 4.15 (2H, s, CH_2), 3.88 (3H, s, CH_3O), 3.85 (3H, s, CH_3O). Anal. Calcd. For $C_{19}H_{17}N_3O_2$: C 71.46, H 5.37, N 13.16. Found: C 71.70, H 5.35, N 13.22.

4-(4-Fluorophenyl)-5*H*-indeno[1,2-*d*]pyrimidin-2-amine (10d). This compound was obtained as yellow crystals, mp 225–227°C; ir (KBr, ν, cm^{-1}): 3482, 3306, 3176, 2890, 1632, 1588, 1566, 1509, 1488, 1463, 1449, 1419, 1394, 1372, 1300, 1279, 1253, 1222; ^1H NMR (400MHz, DMSO-d_6) (δ, ppm): 8.17 (2H, dd, J = 5.6 Hz, J = 5.6 Hz, ArH), 7.92 (1H, d, J = 7.2 Hz, ArH), 7.68 (1H, d, J = 7.2 Hz, ArH), 7.54 (1H, t, J = 7.2 Hz, ArH), 7.49 (1H, t, J = 7.2 Hz, ArH), 7.38 (2H, t, J = 8.8 Hz, ArH), 6.70 (2H, s, NH_2), 4.13 (2H, s, CH_2). Anal. Calcd. For $C_{17}H_{12}FN_3$: C 73.63, H 4.36, N 15.15. Found: C 73.78, H 4.34, N 15.18.

4-(4-Chlorophenyl)-5*H*-indeno[1,2-*d*]pyrimidin-2-amine (10e). This compound was obtained as yellow crystals, mp 237–238°C, Lit. [10f] 245–246°C; ir (KBr, ν, cm^{-1}): 3454, 3302, 3181, 1635, 1592, 1581, 1565, 1545, 1485, 1468, 1453, 1413, 1391, 1369, 1301, 1250, 1212; ^1H NMR (400MHz, DMSO-d_6) (δ, ppm): 8.14 (2H, d, J = 8.8 Hz, ArH), 7.92 (1H, d, J = 7.2 Hz, ArH), 7.69 (1H, d, J = 7.2 Hz, ArH), 7.62 (2H, d, J = 8.4 Hz, ArH), 7.56 (1H, t, J = 7.2 Hz, ArH), 7.49 (1H, t, J = 7.2 Hz, ArH), 6.72 (2H, s, NH_2), 4.13 (2H, s, CH_2). Anal. Calcd. For $C_{17}H_{12}ClN_3$: C 69.51, H 4.12, N 14.30. Found: C 69.69, H 4.20, N 14.21.

4-(4-Bromophenyl)-5*H*-indeno[1,2-*d*]pyrimidin-2-amine (10f). This compound was obtained as yellow crystals, mp 233–234°C, Lit. [10f] 218–219°C; ir (KBr, ν, cm^{-1}): 3455, 3302, 3182, 1634, 1591, 1579, 1562, 1547, 1486, 1468, 1452, 1409, 1388, 1366, 1300, 1251, 1212; ^1H NMR (400MHz, DMSO-d_6) (δ, ppm): 8.07 (2H, d, J = 8.0 Hz, ArH), 7.92 (1H, d, J = 7.6 Hz, ArH), 7.76 (2H, d, J = 8.4 Hz, ArH), 7.69 (1H, d, J = 7.6 Hz, ArH), 7.56 (1H, t, J = 7.2 Hz, J = 7.2 Hz, ArH), 7.50 (1H, t, J = 7.2 Hz, J = 7.2 Hz, ArH), 6.73 (2H, s, NH_2), 4.13 (2H, s, CH_2). Anal. Calcd. For $C_{17}H_{12}BrN_3$: C 60.37, H 3.58, N 12.42. Found: C 60.49, H 3.51, N 12.33.

4-(3,4-Dichlorophenyl)-5*H*-indeno[1,2-*d*]pyrimidin-2-amine (10g). This compound was obtained as yellow crystals, mp 232–233°C; ir (KBr, ν, cm^{-1}): 3481, 3316, 3185, 2903, 1646, 1613, 1592, 1558, 1487, 1469, 1408, 1375, 1361, 1286, 1260, 1245, 1203; ^1H NMR (400MHz, DMSO-d_6) (δ, ppm): 8.33 (1H, d, J = 1.6 Hz, ArH), 8.09 (1H, dd, J = 1.6 Hz, J = 2.0 Hz, ArH), 7.93 (1H, d, J = 7.6 Hz, ArH), 7.81 (1H, d, J = 7.6 Hz, ArH), 7.70 (1H, d, J = 7.6 Hz, ArH), 7.56 (1H, t, J = 7.6 Hz, ArH), 7.52 (1H, t, J = 7.6 Hz, ArH), 6.80 (2H, s, NH_2), 4.16 (2H, s, CH_2). Anal. Calcd. For $C_{17}H_{11}Cl_2N_3$: C 62.21, H 3.38, N 12.80. Found: C 62.35, H 3.36, N 12.77.

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