An Efficient Synthesis of 2,3-Dihydroquinazolin-4(1*H*)-one Derivatives under Catalyst-Free and Solvent-Free Conditions

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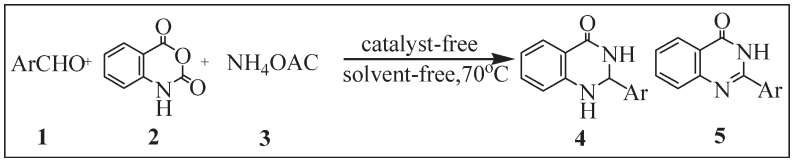

A simple, efficient and convenient one-pot synthesis of 2,3-dihydroquinazolin-4(1*H*)-one derivatives under solvent-free and catalyst-free conditions by the reaction of aromatic aldehydes, isatoic anhydride, and ammonium acetate was reported. The advantages of this protocol include short reaction time, mild reaction conditions, easy work-up, high yields, and environmental friendliness.

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INTRODUCTION

Compounds with biological activity are often derived from heterocyclic structures. Heterocycles are an important class of substrates that are found in natural products such as vitamins, hormones, antibiotics, as well as pharmaceuticals, herbicides, dyes, and many other compounds [1].

2,3-Dihydroquinazolin-4(1*H*)-one derivatives are an important class of heterocycles for pharmaceutical chemistry. They have been reported to exhibit diverse pharmacological activities and biological activities such as antitumor activity, diuretic properties, herbicide activity, and plant growth regulation ability [2].

A number of methods have been reported to prepare 2,3-dihydroquinazolin-4(1*H*)-one derivatives in the past few years. The typical procedure for the synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones involves the condensation reaction of anthranilamide with aldehyde or ketone using *p*-toluenesulfonic acids as a catalyst under vigorous conditions [3]. In 2005, Kurth and coworkers reported a one-pot conversion of 2-nitro-*N*-arylbenzamides to 2,3-dihydroquinazolin-4(1*H*)-ones using 10 equiv $SnCl_2$ in RCH_2OH for 2-day-long refluxing [4]. A recent report described the preparation of 2,3-dihydroquinazolin-4(1*H*)-ones by one-pot synthesis catalyzed by $Ga(OTf)_3$ in ethanol [5]. Salehi and coworkers reported some new one-pot synthesis of these compounds using different catalysts, such as *p*-toluenesulfonic acids [6a], silica sulfuric acid [6b], alum [6c], and Montmorillonite K-10 [6d]. Rostamizadeh *et al*. reported the synthesis of new 2-aryl-substituted 2,3-dihydroquinazolin-4(1*H*)-ones under solvent-free conditions, using molecular iodine as a catalyst at 110°C within 4–25 min [7]. Several years ago, we reported one-pot synthesis of quinazolin-4(3*H*)-ones and 1,2-dihydroquinazolin-4(3*H*)-ones using $TiCl_4$-Zn in anhydrous THF [8]. Some other methods for the synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones involved the condensation of 2-aminobenzamide with aldehydes or ketones in the presence of various catalysts such as $CuCl_2$ [9], NH_4Cl [10], $Sc(OTf)_3$ [11], and SmI_2 [12]. However, many of these methods mentioned above suffer from drawbacks, such as high reaction temperatures, low yields, or toxic solvents. For example, when NH_4Cl [10] was used as catalyst, the starting material 2-aminobenzamide was not easy to get, which must be synthesized with several steps. If the reaction was promoted by $TiCl_4$-Zn [8], it must be proceeded under oxygen-free and anhydrous conditions. Even little amount of oxygen could stop the reaction from happening. When it comes to SmI_2 [12], the raw material was not easily obtained, the reaction must be performed under the protection of dry nitrogen, and the after-treatment of the reaction was complex. It was time consuming and low efficiency to adopt such measures as a result of these severe requirements. Moreover, some catalysts are expensive and not easily available. And above all, the primary disadvantages about the reported methods were that the organic solvent was required, which would pollute our living surroundings.

Because of the growing concern for the influence of the organic solvent on the environment as well as on

human body, organic reactions without using conventional organic solvents are of great significance for synthetic organic chemists today. There has been an upsurge of interest in synthesizing compounds in solvent-free environment during recent years. Compared with the ways used in the solvent, the solvent-free approach proceeded more cleanly and provided higher yields. One-pot transformations, particularly multicomponent reactions (MCRs), are attracting much attention in modern synthetic organic chemistry [13]. It must be an ideal process for MCRs, which can be carried out under solvent-free conditions. Herein, we have designed a three-component one-step synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones under catalyst- and solvent-free conditions.

RESULTS AND DISCUSSION

We carried out the reaction of aromatic aldehyde **1**, isatoic anhydride **2**, and ammonium acetate **3** in a mortar (Scheme 1). The mixture was ground and then heated at 70°C under solvent-free and catalyst-free conditions for about 10 min and the reactions could be completed, and the corresponding 2,3-dihydroquinazolin-4(1*H*)-ones were obtained in excellent yields (Table 1).

Encouraged by this success, we examined the scope and limitations of this approach by applying the optimal reaction conditions to a number of aromatic aldehydes bearing electron-withdrawing and electron-donating substituents. We found that the property of substituent groups of the aromatic aldehydes did not affect these reactions. The results of the reaction are listed in Table 1.

In the course of our study, we found a amusing phenomena: when we use 2-methoxybenzaldehyde and 3,4,5-trimethoxybenzaldehyde, we obtained the products 2-arylquin-azolin-4(3*H*)-one **5**; however, we did not gain corresponding products 2-aryl-2,3-dihydroquinazolin-4(1*H*)-one **4**. Although we tried many times using the same reagents, the results were the same. The structures of all the products were confirmed on the basis of spectroscopic data, particularly ^{1}H-NMR analysis and HRMS spectra.

In conclusion, in this article, we have developed a successful protocol for the efficient and facile synthesis of 2,3-dihydroquinazolin-4(1*H*)-one derivatives *via* the one-pot reaction under solvent-free conditions. High efficiency, easy availability, low cost, operational simplicity, mild reaction conditions, and improved yields are the advantages of this new method. Moreover, the products were performed in excellent yields within short reaction times. It is worth noting that the primary highlight of this method lies in that it did not use any toxic solvent and any catalyst in the reaction. Starting materials are also inexpensive and commercially available.

Scheme 1

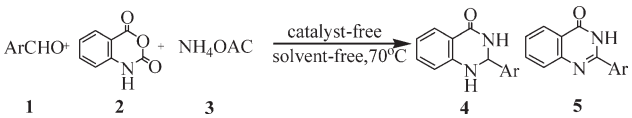

Table 1

The results of synthesis of 2,3-dihydroquinazolin-4(1*H*)-one.

Entry	Ar	Product	Yields (%)
1	4-BrC_6H_4	**4a**	90
2	4-FC_6H_4	**4b**	95
3	4-$CH_3C_6H_4$	**4c**	96
4	4-$CH_3OC_6H_4$	**4d**	98
5	3-ClC_6H_4	**4e**	89
6	3-BrC_6H_4	**4f**	87
7	3,4-$(CH_3)_2C_6H_3$	**4g**	94
8	2-ClC_6H_4	**4h**	90
9	4-ClC_6H_4	**4i**	96
10	C_6H_5	**4j**	91
11	2,5-$(CH_3O)_2C_6H_3$	**4k**	94
12	3,4-$(CH_3O)_2C_6H_3$	**4l**	92
13	4-pyridyl	**4m**	89
14	2-$CH_3OC_6H_4$	**5a**	95
15	3,4,5-$(CH_3O)_3C_6H_2$	**5b**	88

EXPERIMENTAL

Melting points were determined on XT-5 microscopic melting point apparatus and were uncorrected. IR spectra were recorded on a FTIR-8101 spectrometer. ^{1}H-NMR spectra were obtained from solution in DMSO-d_6 with Me_4Si as an internal standard using a Bruker-400 spectrometer. Microanalyses were carried out using a Perkin-Elmer 2400 II analyzer. HRMS spectra were obtained with a Bruker micrOTOF-Q 134 instrument.

General procedure for the synthesis of 2,3-dihydroquinazolin-4(1*H*)-one derivatives. A round-bottom flask was charged with aromatic aldehydes **1** (2 mmol), isatoic anhydride **2** (2 mmol), and ammonium acetate **3** (3 mmol). The mixture was heated at ~70°C over the course of 10 min. After the reaction was completed, the reaction mixture was poured into water and then washed with water thoroughly. The product was filtered, dried, and recrystallized from 95% ethanol.

2-(4-Bromophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (4a). m.p. 202–204°C; IR (KBr, ν, cm^{-1}): 3309, 3190, 3065, 1655, 1609, 1509, 1485, 1433, 1385, 1293, 1153, 1014, 753, 679, 668 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 5.76 (1H, s, CH), 6.69 (1H, t, J = 7.2 Hz, J = 7.6 Hz, ArH), 6.75 (1H, d, J = 8.0 Hz, ArH), 7.16 (1H, s, NH), 7.26 (1H, t, J = 8.4 Hz, ArH), 7.44 (2H, d, J = 8.4 Hz, ArH), 7.60 (3H, d, J = 8.4 Hz, ArH), 8.35 (1H, s, NH); Anal. Calcd. for $C_{14}H_{11}BrN_2O$: C, 55.47; H, 3.66; N, 9.24. Found: C, 55.40; H, 3.68; N, 9.30. HRMS *m/z* calculated for $C_{14}H_{11}BrN_2O$ [M+Na]: 324.9952, found: 324.9947.

2-(4-Fluorophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (4b). m.p. 197–199°C; IR (KBr, ν, cm^{-1}): 3302, 3184, 3068, 1653, 1613, 1509, 1487, 1439, 1389, 1300, 1234, 1157, 842,

811, 747, 670 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 5.78 (1H, s, CH), 6.69 (1H, t, J = 7.6 Hz, J = 7.2 Hz, ArH), 6.75 (1H, d, J = 8.4 Hz, ArH), 7.10 (1H, s, NH), 7.23 (3H, t, J = 8.8 Hz, ArH), 7.54 (2H, dd, J = 5.6 Hz, J = 5.6 Hz, ArH), 7.62 (1H, d, J = 7.6 Hz, ArH), 8.30 (1H, s, NH); Anal. Calcd. for $C_{14}H_{11}FN_2O$: C, 69.41; H, 4.58; N, 11.56. Found: C, 69.50; H, 4.54; N, 11.51. HRMS *m/z* calculated for $C_{14}H_{11}FN_2O$ [M+Na]: 265.0753, found: 265.0768.

2-*p*-Tolyl-2,3-dihydroquinazolin-4(1*H*)-one (4c). m.p. 221–223°C; IR (KBr, ν, cm^{-1}): 3312, 3195, 3065, 1656, 1611, 1542, 1509, 1487, 1437, 1297, 1151, 752, 669, 657 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 2.30 (3H, s, CH_3), 5.71 (1H, s, CH), 6.67 (1H, t, J = 7.6 Hz, J = 7.6 Hz, ArH), 6.74 (1H, d, J = 8.0 Hz, ArH), 7.07 (1H, s, NH), 7.19 (2H, d, J = 8.0 Hz, ArH), 7.24 (1H, t, J = 8.4 Hz, ArH), 7.37 (2H, d, J = 8.0 Hz, ArH), 7.60 (1H, d, J = 7.6 Hz, ArH), 8.25 (1H, s, NH); Anal. Calcd. for $C_{15}H_{14}N_2O$: C, 75.61; H, 5.92; N, 11.76. Found: C, 75.73; H, 5.96; N, 11.70. HRMS *m/z* calculated for $C_{15}H_{14}N_2O$ [M+Na]: 261.1004, found: 261.1002.

2-(4-Methoxyphenyl)-2,3-dihydroquinazolin-4(1*H*)-one (4d). m.p. 189–191°C; IR (KBr, ν, cm^{-1}): 3300, 3185, 3053, 1654, 1613, 1509, 1488, 1438, 1390, 1305, 1255, 1033, 836, 806, 758, 669 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 3.75 (3H, s, OCH_3), 5.71 (1H, s, CH), 6.68 (1H, t, J = 7.6 Hz, J = 7.2 Hz, ArH), 6.74 (1H, d, J = 8.4 Hz, ArH), 6.95 (2H, d, J = 8.8 Hz, ArH), 7.01 (1H, s, NH), 7.24 (1H, t, J = 8.4 Hz, ArH), 7.42 (2H, d, J = 8.8 Hz, ArH), 7.61 (1H, dd, J = 1.2 Hz, J = 1.2 Hz, ArH), 8.19 (1H, s, NH); Anal. Calcd. for $C_{15}H_{14}N_2O_2$: C, 70.85; H, 5.55; N, 11.02. Found: C, 70.67; H, 5.57; N, 11.05. HRMS *m/z* calculated for $C_{15}H_{14}N_2O_2$ [M+Na]: 277.0953, found: 277.0969.

2-(3-Chlorophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (4e). m.p. 185–186°C; IR (KBr, ν, cm^{-1}): 3291, 3198, 3067, 1650, 1614, 1514, 1487, 1436, 1387, 1340, 1299, 1201, 1157, 871, 818, 793, 756, 699, 667 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 5.78 (1H, s, CH), 6.69 (1H, t, J = 7.6 Hz, J = 7.2 Hz, ArH), 6.76 (1H, d, J = 8.0 Hz, ArH), 7.22 (1H, s, ArH), 7.26 (1H, t, J = 8.4 Hz, ArH), 7.42 (3H, m, ArH), 7.53 (1H, s, NH), 7.61 (1H, dd, J = 1.2 Hz, J = 1.2 Hz, ArH), 8.40 (1H, s, NH); Anal. Calcd. for $C_{14}H_{11}ClN_2O$: C, 65.00; H, 4.29; N, 10.83. Found: C, 65.35; H, 4.33; N, 10.79. HRMS *m/z* calculated for $C_{14}H_{11}ClN_2O$ [M+Na]: 281.0458, found: 281.0482.

2-(3-Bromophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (4f). m.p. 179–181°C; IR (KBr, ν, cm^{-1}): 3271, 3182, 3057, 1650, 1615, 1509, 1433, 1389, 1298, 1264, 1150, 888, 752, 698, 613 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 5.67 (1H, s, CH), 6.69 (1H, t, J = 7.6 Hz, J = 7.2 Hz, ArH), 6.76 (1H, d, J = 8.0 Hz, ArH), 7.23 (1H, s, ArH), 7.26 (1H, t, J = 8.4 Hz, ArH), 7.36 (1H, t, J = 7.6 Hz, J = 8.0 Hz, ArH), 7.49 (1H, d, J = 7.6 Hz, ArH), 7.54 (1H, d, J = 9.2 Hz, ArH), 7.61 (1H, d, J = 1.2 Hz, ArH), 7.67 (1H, s, NH), 8.52 (1H, s, NH); Anal. Calcd. for $C_{14}H_{11}BrN_2O$: C, 55.47; H, 3.66; N, 9.24. Found: C, 55.53; H, 3.63; N, 9.19. HRMS *m/z* calculated for $C_{14}H_{11}BrN_2O$ [M+Na]: 324.9952, found: 324.9945.

2-(3,4-Dimethylphenyl)-2,3-dihydroquinazolin-4(1*H*)-one (4g). m.p. 186–188°C; IR (KBr, ν, cm^{-1}): 3294, 3193, 3068, 1651, 1615, 1516, 1488, 1447, 1386, 1334, 1299, 1152, 1132, 829, 808, 755, 657, 624 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 2.30 (3H, s, CH_3), 2.32 (3H, s, CH_3), 5.67 (1H, s, CH), 7.11 (1H, s, NH), 7.31 (1H, d, J = 8.0 Hz, ArH), 7.51 (1H, t, J = 7.6 Hz, J = 7.2 Hz, ArH), 7.74 (1H, d, J = 8.0 Hz, ArH), 7.84 (1H, t, J = 8.0 Hz, J = 8.4 Hz, ArH), 7.92 (1H, d, J = 7.6 Hz, ArH), 8.01 (1H, s, ArH), 8.15 (1H, d, J = 0.8 Hz, ArH), 8.53 (1H, s, NH); ^{13}C-NMR (400 MHz, DMSO-d_6) (δ, ppm): 163.6, 147.9, 138.9, 136.4, 135.9, 133.2, 129.3, 128.0, 127.3, 124.2, 117.0, 115.0, 114.4, 66.5, 19.4, 19.0; Anal. Calcd. for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.39; N, 11.10. Found: C, 76.32; H, 6.35; N, 11.14. HRMS *m/z* calculated for $C_{16}H_{16}N_2O$ [M+Na]: 275.1160, found: 275.1188.

2-(2-Chlorophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (4h). m.p. 204–206°C; IR (KBr, ν, cm^{-1}): 3362, 3196, 3066, 1648, 1615, 1505, 1395, 1352, 1330, 1353, 1189, 1155, 1123, 746, 669, 618 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 6.14 (1H, s, CH), 6.72 (1H, t, J = 7.2 Hz, J = 7.6 Hz, ArH), 6.76 (1H, d, J = 8.0 Hz, ArH), 7.03 (1H, s, NH), 7.27 (1H, t, J = 8.4 Hz, ArH), 7.39–7.43 (2H, m, ArH), 7.48–7.52 (1H, m, ArH), 7.66 (2H, d, J = 6.0 Hz, ArH), 8.23 (1H, s, NH); ^{13}C-NMR (400 MHz, DMSO-d_6) (δ, ppm): 163.6, 147.6, 137.9,133.4, 131.8, 130.2, 129.6, 128.7, 127.4, 127.3, 117.4, 114.7, 114.5, 63.7; Anal. Calcd. for $C_{14}H_{11}ClN_2O$: C, 65.00; H, 4.29; N, 10.83. Found: C, 65.30; H, 4.32; N, 10.77. HRMS *m/z* calculated for $C_{14}H_{11}ClN_2O$ [M+Na]: 281.0458, found: 281.0476.

2-(4-Chlorophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (4i). m.p. 197–199°C; IR (KBr, ν, cm^{-1}): 3309, 3188, 3066, 1655, 1611, 1509, 1486, 1386, 1293, 1153, 1093, 1017, 837, 801, 753, 669 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 5.77 (1H, s, CH), 6.69 (1H, t, J = 7.2 Hz, J = 7.6 Hz, ArH), 6.75 (1H, d, J = 8.0 Hz, ArH), 7.15 (1H, s, NH), 7.26 (1H, t, J = 7.6 Hz, J = 8.8 Hz, ArH), 7.49 (3H, dd, J = 8.8 Hz, J = 8.8 Hz, ArH), 7.62 (2H, d, J = 8.8 Hz, ArH), 8.35 (1H, s, NH); Anal. Calcd. for $C_{14}H_{11}ClN_2O$: C, 65.00; H, 4.29; N, 10.83. Found: C, 65.35; H, 4.25; N, 10.78. HRMS *m/z* calculated for $C_{14}H_{11}ClN_2O$ [M+Na]: 281.0458, found: 281.0460.

2-Phenyl-2,3-dihydroquinazolin-4(1*H*)-one (4j). m.p. 223–224°C; IR (KBr, ν, cm^{-1}): 3304, 3188, 1668, 1652, 1615, 1507, 1487, 1455, 1393, 1300, 1149, 748, 699, 667, 643 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 5.76 (1H, s, CH), 6.68 (1H, t, J = 7.2 Hz, ArH), 6.75 (1H, d, J = 8.0 Hz, ArH), 7.14 (1H, s, NH), 7.25 (1H, t, J = 8.4 Hz, ArH), 7.35–7.42 (3H, m, ArH), 7.50 (2H, d, J = 6.8 Hz, ArH), 7.62 (1H, dd, J = 1.2 Hz, J = 1.2 Hz, ArH), 8.32 (1H, s, NH); Anal. Calcd. for $C_{14}H_{12}N_2O$: C, 74.98; H, 5.39; N, 12.49. Found: C, 74.70; H, 5.41; N, 12.43. HRMS *m/z* calculated for $C_{14}H_{12}N_2O$ [M+Na]: 247.0847, found: 247.0843.

2-(2,5-Dimethoxyphenyl)-2,3-dihydroquinazolin-4(1*H*)-one (4k). m.p. 164–165°C; IR (KBr, ν, cm^{-1}): 3198, 3102, 1651, 1610, 1577, 1498, 1457, 1357, 1310, 1282, 1250, 1220, 1122, 1051, 759, 702 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 3.67 (3H, s, OCH_3), 3.79 (3H, s, OCH_3), 5.99 (1H, s, CH), 6.68 (1H, t, J = 7.2 Hz, J = 7.6 Hz, ArH), 6.78 (1H, d, J = 8.0 Hz, ArH), 6.82 (1H, s, NH), 6.89 (1H, dd, J = 3.2 Hz, J = 3.2 Hz, ArH), 6.95–7.00 (2H, m, ArH), 7.24 (1H, t, J = 7.2 Hz, J = 7.6 Hz, ArH), 7.63 (1H, d, J = 7.6 Hz, ArH), 8.06 (1H, s, NH); ^{13}C-NMR (400 MHz, DMSO-d_6) (δ, ppm): 163.8, 152.9, 150.5, 147.9, 133.2, 129.9, 127.3, 117.1, 114.8, 114.5, 113.5, 113.4, 112.2, 61.0, 56.0, 55.4; Anal. Calcd. for $C_{16}H_{16}N_2O_3$: C, 67.59; H, 5.67; N, 9.85. Found: C, 67.50; H, 5.62; N, 9.89. HRMS *m/z* calculated for $C_{16}H_{16}N_2O_3$ [M+Na]: 307.1059, found: 307.1061.

2-(3,4-Dimethoxyphenyl)-2,3-dihydroquinazolin-4(1*H*)-one (4l). m.p. 208–210°C; IR (KBr, ν, cm^{-1}): 3354, 3333, 1671, 1609, 1557, 1539, 1516, 1496, 1480, 1456, 1415, 1363, 1318, 1269, 1227, 1144, 1015, 854, 769, 702 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 3.58 (3H, s, OCH_3), 3.60 (3H, s, OCH_3), 5.54 (1H, s, CH), 6.52 (1H, t, J = 7.2 Hz, J = 7.6 Hz, ArH), 6.60 (1H, d, J = 8.0 Hz, ArH), 6.79 (1H, d, J = 8.4 Hz, ArH), 6.85 (1H, d, J = 8.0 Hz, ArH), 6.88 (1H, s, NH), 6.97 (1H, s, ArH), 7.09 (1H, t, J = 8.4 Hz, J = 8.4 Hz, ArH), 7.46 (1H, dd, J = 1.2 Hz, J = 1.2 Hz, ArH), 8.05 (1H, s, NH); Anal. Calcd. for $C_{16}H_{16}N_2O_3$: C, 67.59; H, 5.67; N, 9.85. Found: C, 67.61; H, 5.70; N, 9.91. HRMS *m/z* calculated for $C_{16}H_{16}N_2O_3$ [M+Na]: 307.1059, found: 307.1059.

2-(Pyridin-4-yl)-2,3-dihydroquinazolin-4(1*H*)-one (4m). m.p. 264–265°C; IR (KBr, ν, cm^{-1}): 3207, 2957, 1678, 1648, 1599, 1570, 1559, 1489, 1468, 1449, 1304, 1189, 772, 699 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 7.53–7.63 (2H, m, ArH, CH), 7.80 (1H, d, J = 8.0 Hz, ArH), 7.89 (1H, t, J = 7.2 Hz, J = 7.6 Hz, CH), 8.12 (2H, d, J = 6.0 Hz, ArH), 8.19 (1H, d, J = 7.6 Hz, NH), 8.72 (1H, s, NH), 8.80 (2H, d, J = 5.6 Hz, ArH), 12.81 (1H, s, NH); Anal. Calcd. for $C_{13}H_{11}N_3O$: C, 69.32; H, 4.92; N, 18.66; O, 7.10. Found: C, 69.46; H, 4.89; N, 18.69. HRMS *m/z* calculated for $C_{13}H_{11}N_3O$ [M+Na]: 248.0800, found: 248.0802.

2-(2-Methoxyphenyl)quinazolin-4(3*H*)-one (5a). m.p. 202–203°C; IR (KBr, ν, cm^{-1}): 3321, 3095, 1681, 1592, 1558, 1478, 1456, 1302, 1235, 1186, 1138, 1016, 759, 744 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 3.86 (3H, s, OCH_3), 7.10 (1H, t, J = 7.6 Hz, ArH), 7.20 (1H, d, J = 8.4 Hz, ArH), 7.54 (2H, t, J = 6.8 Hz, ArH), 7.71 (2H, d, J = 8.0 Hz, ArH), 7.84 (1H, t, J = 7.6 Hz, ArH), 8.16 (1H, d, J = 7.6 Hz, ArH), 12.14 (1H, s, NH); ^{13}C-NMR (400 MHz, DMSO-d_6) (δ, ppm): 163.8, 156.4, 147.9, 133.2, 129.6, 129.0, 127.3, 126.8, 120.1, 116.9, 114.7, 114.5, 111.1, 61.0, 55.5; Anal. Calcd. for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.51; H, 4.73; N, 11.14. HRMS *m/z* calculated for $C_{15}H_{12}N_2O_2$ [M+Na]: 275.0796, found: 275.0798.

2-(3,4,5-Trimethoxyphenyl)quinazolin-4(3*H*)-one (5b). m.p. 254–256°C; IR (KBr, ν, cm^{-1}): 3202, 2936, 1669, 1605, 1574, 1521, 1482, 1457, 1342, 1284, 1235, 1140, 999, 857, 840, 774, 722 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 3.75 (3H, s, OCH_3), 3.91 (6H, s, 2×OCH_3), 7.53 (1H, t, J = 7.6 Hz, J = 7.2 Hz, ArH), 7.57 (2H, s, ArH), 7.76 (1H, d, J = 8.0 Hz, ArH), 7.85 (1H, t, J = 7.6 Hz, J = 8.4 Hz, ArH), 8.16 (1H, d, J = 7.6 Hz, ArH), 12.56 (1H, s, NH); ^{13}C-NMR (400 MHz, DMSO-d_6) (δ, ppm): 162.2, 158.5, 158.1, 152.9, 152.0, 148.1, 140.4, 134.7, 127.3, 127.0, 126.5, 125.9, 120.7, 113.7, 105.4, 60.2, 56.2; Anal. Calcd. for $C_{17}H_{16}N_2O_4$: C, 65.38; H, 5.16; N, 8.97. Found: C, 65.55; H, 5.20; N, 8.92. HRMS *m/z* calculated for $C_{17}H_{16}N_2O_4$ [M+Na]: 335.1008, found: 335.1005.

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REFERENCES AND NOTES

[1] Dou, G. L.; Shi, D. Q.; Li, Y. H. J Comb Chem 2010, 12, 195.

[2] (a) Hamel, E.; Lin, C. M.; Plowman, J.; Wang, H.; Lee, K.; Paull, K. D. Biochem Pharmacol 1996, 51, 53; (b) Biressi, M. G.; Cantarelli, G.; Carissimi, M.; Cattaneo, A.; Ravenna, F. Farmaco Ed Sci 1969, 24, 199; (c) Bhalla, P. R.; Walworth, B. L. American Cyanamid Co. Eur. Pat. Appl. EP58.822 (1982); (c) Bhalla, P. R.; Walworth, B. L. Chem. Abstr. 1983, 98, 1669; (d) Bhalla, P. R.; Walworth, B. L. American Cyanamid Co. U.S. Pat. 4,431,440 (1984); (d) Bhalla, P. R.; Walworth, B. L. Chem. Abstr. 1984, 100, 174857; (e) Hour, M.; Huang, L.; Kuo, S.; Xia, Y.; Bastow, K.; Nakanishi, Y.; Hamel, E.; Lee, K. J Med Chem 2000, 43, 4479.

[3] (a) Moore, J. A.; Sutherland, G. J.; Sowerby, R.; Kelly, E. G.; Palermo, S.; Webdter, W. J Org Chem 1969, 34, 887; (b) Sharma, S. D.; Kaur, V. Synthesis 1989, 677.

[4] Yoo, C. L.; Fettinger, J. C.; Kurth, M. J. J Org Chem 2005, 70, 6941.

[5] Chen, J. X.; Wu, D. Z.; He, F.; Liu, M. C.; Wu, H. Y.; Ding, J. C.; Su, W. K. Tetrahedron Lett 2008, 49, 3817.

[6] (a) Baghbanzadeh, M.; Salehi, P.; Dabiri, M.; Kozehgarya, G. Synthesis 2006, 344; (b) Salehi, P.; Dabiri, M.; Zolfigol, M. A.; Baghbanzadeh, M. Synlett 2005, 1155; (c) Dabiri, M.; Salehi, P.; Otokesh, S.; Baghbanzadeh, M.; Kozehgarya, G.; Mohammadi, A. A. Tetrahedron Lett 2005, 46, 6123; (d) Salehi, P.; Dabiri, M.; Baghbanzadeh, M.; Bahramnejad, M. Synth Commun 2006, 36, 2287.

[7] Rostamizadeh, S.; Amani, A. M.; Aryan, R.; Ghaieni, H. R.; Shadjou, N. Synth Commun 2008, 38, 3569.

[8] Shi, D. Q.; Rong, L. C.; Wang, J. X.; Zhuang, Q. Y.; Wang, X. S.; Hu, H. W. Tetrahedron Lett 2003, 44, 3199.

[9] Abdel-Jalil, R. J.; Voelter, W.; Saeed, M. Tetrahedron Lett 2004, 45, 3475.

[10] Shaabani, A.; Maleki, A.; Mofakham, H. Synth Commun 2008, 38, 3752.

[11] Chen, J. X.; Wu, H. Y.; Su, W. K. Chin Chem Lett 2007, 18, 537.

[12] Su, W. K.; Yang, B. B. Aust J Chem 2002, 55, 695.

[13] (a) Pandey, G.; Singh, R. P.; Gary, A.; Singh, V. K. Tetrahedron Lett 2005, 46, 2137; (b) Werner, B.; Domling, A. Molecules 2003, 8, 53; (c) Domling, A.; Ugi, I. Angew Chem Int Ed 2000, 39, 3169; (d) Kappe, C. O. Acc Chem Res 2000, 33, 879.