



Polyethylene glycol (PEG-400) as a medium for novel and efficient synthesis of 2-phenyl-2,3-dihydroquinazolin-4(1*H*)-one derivatives

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ABSTRACT

A novel, efficient synthesis of 2-phenyl-2, 3-dihydroquinazolin-4(1*H*)-one derivatives is reported for the first time in PEG-400 by the reaction of various aldehydes, anthranilamide under catalyst-free conditions and the formation of product good to excellent yields. PEG-400 can be recovered and reused without any significant loss of activity.

1. Introduction

2,3-Dihydroquinazolin-4(1*H*)-one derivatives are playing crucial role in the context of drug intermediates, biological and pharmaceutical applications. Its analogues are widely used in heterocyclic chemistry, medicinal chemistry [1]. These derivatives exhibit good biological activities such as anticancer, antitumor, diuretic, herbicidal, and plant growth regulation [2]. They are some marketed drugs with quinazolinone skeleton are given in Figure 1. Numerous methods have been reported for the synthesis 2,3-dihydroquinazolin-4(1*H*)-one derivatives by using different catalytic mediums such as $KAl(SO_4)_2 \cdot 12H_2O$ [3], molecular iodine [4], ionic liquids ([bmim]BF₄) [5], montmorillonite K-10 [6], gallium(III)triflate [7], MCM-41-SO₃H [8], silica sulfuric acid [9], Al(H₂PO₄)₃ [10], and zinc(II)perfluorooctanoate [Zn(PFO)₂] [11]. Wang *et al.* developed the aqueous phase synthesis of 2-substituted-2,3-dihydroquinazolin-4(1*H*)-ones from anthranilamide and different aldehydes/ketones [12]. Singh and co-workers reported the synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones from isatoic anhydride, aldehyde, amine or ammonium acetate in water under microwave in the presence of L-proline [13]. Arjmandi and co-workers described the acetic acid mediated synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones from isatoic anhydride, aldehyde, amine [14]. Recently, Ramesh and co-workers demonstrated the synthesis of 2-phenyl-2,3-dihydroquinazolin-4(1*H*)-ones from anthranilamide, different aldehydes in the presence of β -cyclodextrin water [15]. The above mentioned methods suffered from one or more disadvantages such as the use of hazardous organic solvents, low yields, strongly acidic conditions, expensive moisture-sensitive catalysts, and tedious workup conditions. In past decades, polyethylene glycol (PEG-400) has acquired significance as an eco-friendly solvent in many organic reactions, and economically viable, non-hazardous, and

nontoxic green solvent. On the other hand, PEG also acts as a phase transfer catalyst and is used in many synthetic organic transformations [16] such as oxidation, reduction reactions [17], and Suzuki cross-coupling reaction [18], Wacker reaction [19], and Heck reaction [20].

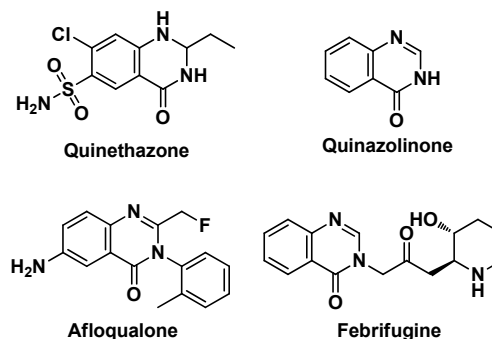
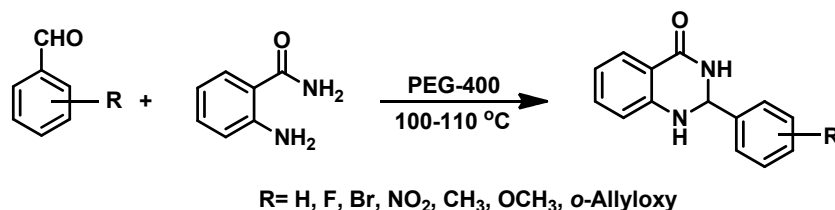


Figure 1. Some marketed drugs with quinazolinone skeleton.

2. Experimental

2.1. Instrumentation and material

All the chemicals were purchased from Sigma Aldrich with purity not less than 99.9%. Analytical thin layer chromatography (TLC) was carried out by using silica gel 60F₂₅₄ pre-coated plates. Visualization was accomplished with UV lamp of I₂ stain. All the products were characterized by their NMR and Mass spectra. ¹H NMR and ¹³C NMR were recorded on 200 or 300 MHz, in CDCl₃, and the chemical shifts were reported in parts per million (ppm, δ) downfield from the tetramethylsilane.



Scheme 1. Synthesis of 2-phenyl-2,3-dihydroquinazolin-4(1H)-one derivatives.

All reactions were carried out without any special precautions in an atmosphere of air. Chemicals were purchased from Fluka and S. D. Fine Chemicals and directly used for the synthesis. TLC: pre-coated silica gel plates (60F₂₅₄, 0.2 mm layer; E. Merck). M.p.: Fischer-Johns melting-point apparatus; uncorrected. ¹H NMR Spectra: Varian 200 or Avance 300 spectrometer; in CDCl₃; δ in ppm, J in Hz, Mass spectra: VG Autospec; in m/z.

2.2. Synthesis

To a stirred solution of polyethylene glycol (5 mL), anthranilamide (1.0 mmol), and aldehyde (1.0 mmol) were added and stirred at 100-110 °C, for an appropriate time. After completion of the reaction, as indicated by TLC, the reaction mass was extracted with ethyl acetate (3 x 10 mL) and PEG was separated. The combined organic layers were evaporated under reduced pressure, and the crude product was purified by column chromatography by using hexane:EtOAc mixture (7:3). The recovered PEG was reused for three cycles without any significant loss of activity (Scheme 1).

2-Phenyl-2,3-dihydroquinazolin-4(1H)-one (Entry 1): Color: White. Yield: 85%. M.p.: 225-227 °C. FT-IR (KBr, ν, cm⁻¹): 3302 (NH), 3184 (NH), 3061 (CH) (NH-CH-NH), 2924 (C=C-H), 1658 (C=O) 1612 (CONH). ¹H NMR (300 MHz, CDCl₃, δ, ppm): 7.95 (d, J = 7.5 Hz, 1H, Ar-H), 7.60-7.57 (m, 2H, Ar-H), 7.48-7.45 (m, 2H, Ar-H), 7.36-7.30 (m, 1H, Ar-H), 7.27 (s, 1H, Ar-H), 6.92 (t, J = 6.7 Hz, 1H, Ar-H), 6.65 (d, J = 7.5 Hz, 1H, Ar-H), 5.92 (s, 1H, -NH-CH-NH), 5.79 (s, 1H, br, -CH-NH-CO), 4.38 (s, 1H, br, Ar-NH-CH-). ¹³C NMR (50 MHz, CDCl₃, δ, ppm): 164.75 (1C, Ar-CO), 147.22 (2C, Ar-C), 138.51 (1C, Ar-C), 134.02 (1C, Ar-C), 130.16 (1C, Ar-C), 129.12 (1C, Ar-C), 128.72 (2C, Ar-C), 127.39 (1C, Ar-C), 119.67 (2C, Ar-C), 114.55 (1C, Ar-C), 69.07 (1C, NH-CH-NH). MS (EI, m/z (%)): 225 [M⁺, 100].

2-(Anthracen-9-yl)-2,3-dihydroquinazolin-4(1H)-one (Entry 2): Color: White. Yield: 85%. M.p.: 235-237 °C. FT-IR (KBr, ν, cm⁻¹): 3304 (NH), 3188 (NH), 3062 (CH) (NH-CH-NH), 2926 (C=C-H), 1657 (C=O) 1611 (CONH). ¹H NMR (300 MHz, CDCl₃, δ, ppm): 8.55 (s, 1H, Ar-H), 8.08-8.02 (m, 3H, Ar-H), 7.52-7.35 (m, 6H, Ar-H), 7.25 (m, 2H, Ar-H), 6.97 (t, J = 6.7 Hz, 1H, Ar-H), 6.68 (d, J = 8.3 Hz, 1H, Ar-H), 6.23 (s, 1H, Ar-H), 4.64 (s, 1H, -NH-CH-Ar). ¹³C NMR (50 MHz, CDCl₃, δ, ppm): 162.22 (1C, Ar-CO), 130.87 (8C, Ar-C), 129.26 (5C, Ar-C), 125.35 (5C, Ar-C), 114.72 (2C, Ar-C), 63.88 (1C, NH-CH-NH). MS (EI, m/z (%)): 325 [M⁺, 100]. Anal. calcd. for (C₂₂H₁₆N₂O): C, 81.46; H, 4.97; N, 8.64. Found: C, 81.40; H, 4.91; N, 8.60%.

2-(4-Nitrophenyl)-2,3-dihydroquinazolin-4(1H)-one (Entry 3): Color: Yellow solid. Yield: 92%. M.p.: 204-206 °C. FT-IR (KBr, ν, cm⁻¹): 3278 (NH), 3174 (NH), 3032 (CH) (NH-CH-NH), 2922 (C=C-H), 1647 (C=O), 1608 (CONH-), 1520 (C=C), 1461 (C=C), 1345 (C=C). ¹H NMR (300 MHz, CDCl₃, δ, ppm): 8.32 (d, J = 8.3 Hz, 1H, Ar-H), 7.97 (m, 1H, Ar-H), 7.84-7.80 (m, 2H, Ar-H), 7.42-7.36 (m, 1H, Ar-H), 7.28 (s, 1H, Ar-H), 6.99-6.91 (m, 1H, Ar-H), 6.71 (d, J = 7.5 Hz, 1H, Ar-H), 6.16 (s, 1H, br, -NH-CO-), 6.04 (s, 1H), 4.42 (s, 1H, br, -NH-CH-NH). ¹³C NMR (50 MHz, CDCl₃, δ, ppm): 162.97 (1C, Ar-CO), 147.61 (1C, Ar-C), 146.51 (1C, Ar-C), 145.96 (1C, Ar-C), 132.45 (2C, Ar-C), 126.79 (1C, Ar-

C), 126.50 (2C, Ar-C), 122.26 (1C, Ar-C), 116.71 (2C, Ar-C), 113.72 (1C, Ar-C), 64.88 (1C, -NH-CH-NH-). MS (EI, m/z (%)): 270 [M⁺, 100].

2-(3-Nitrophenyl)-2,3-dihydroquinazolin-4(1H)-one (Entry 4): Color: Yellow solid. Yield: 88%. M.p.: 210-212 °C. FT-IR (KBr, ν, cm⁻¹): 3293 (NH), 3190 (NH), 3072 (CH) (NH-CH-NH), 2924 (C=C-H), 1654 (C=O) 1608 (CONH), 1533 (C=C), 1461 (C=C), 1345 (C=C). ¹H NMR (300 MHz, CDCl₃, δ, ppm): 8.46 (s, 1H, Ar-H), 8.31 (d, J = 7.9 Hz, 1H, Ar-H), 7.98 (t, J = 7.9 Hz, 2H, Ar-H), 7.67 (t, J = 7.9 Hz, 1H, Ar-H), 7.38 (t, J = 6.9 Hz, 1H, Ar-H), 6.96 (t, J = 6.9 Hz, 1H, Ar-H), 6.71 (d, J = 7.9 Hz, 1H, Ar-H), 6.06 (s, 1H, NH-CH-NH), 5.92 (s, 1H, -NH-CO), 4.43 (s, 1H, NH-CH-Ar). ¹³C NMR (50 MHz, CDCl₃, δ, ppm): 163.22 (1C, Ar-CO), 146.99 (1C, Ar-C), 146.13 (1C, Ar-C), 142.75 (1C, Ar-C), 132.58 (1C, Ar-C), 132.14 (1C, Ar-C), 128.51 (1C, Ar-C), 126.67 (1C, Ar-C), 122.25 (1C, Ar-C), 120.93 (1C, Ar-C), 116.98 (1C, Ar-C), 114.03 (1C, Ar-C), 113.68 (1C, Ar-C), 65.09 (1C, -NH-CH-NH-). MS (EI, m/z (%)): 270 [M⁺, 100].

2-(4-Fluorophenyl)-2,3-dihydroquinazolin-4(1H)-one (Entry 5): Color: White. Yield: 88%. M.p.: 203-204 °C. FT-IR (KBr, ν, cm⁻¹): 3300 (NH), 3183 (NH), 3066 (CH) (NH-CH-NH), 2929 (C=C-H), 1658 (C=O), 1610 (CONH), 1508 (C=C), 1482 (C=C), 1345 (C=C). ¹H NMR (300 MHz, CDCl₃, δ, ppm): 7.95 (d, 1H, J = 8.3 Hz, Ar-H), 7.63-7.58 (m, 2H, Ar-H), 7.38-7.33 (m, 1H, Ar-H), 7.15 (t, J = 8.3 Hz, 2H, Ar-H), 6.93 (t, J = 8.3 Hz, 1H, Ar-H), 6.67 (d, J = 8.3 Hz, 1H, Ar-H), 5.92 (s, 1H, -NH-CH-NH), 5.79 (s, 1H, -NH-CO), 4.35 (s, 1H, -NH-CH-Ar). ¹³C NMR (50 MHz, CDCl₃, δ, ppm): 161.88 (1C, Ar-CO), 158.68 (1C, Ar-C), 146.94 (1C, Ar-C), 132.65 (2C, Ar-C), 128.28 (2C, Ar-C), 128.19 (1C, Ar-C), 126.87 (1C, Ar-C), 117.84 (1C, Ar-C), 114.53 (1C, Ar-C), 114.25 (1C, Ar-C), 113.76 (1C, Ar-C), 66.38 (1C, NH-CH-NH). MS (EI, m/z (%)): 243 [M⁺, 100].

2-(4-Bromophenyl)-2,3-dihydroquinazolin-4(1H)-one (Entry 6): Color: White. Yield: 89%. M.p.: 200-202 °C. FT-IR (KBr, ν, cm⁻¹): 3306 (NH), 3188 (NH), 3060 (CH) (NH-CH-NH), 2927 (C=C-H), 1658 (C=O) 1607 (CONH), 1533 (C=C), 1461 (C=C), 1345 (C=C). ¹H NMR (300 MHz, CDCl₃, δ, ppm): 7.91 (d, 1H, J = 7.1 Hz, Ar-H), 7.53 (d, 2H, J = 8.0 Hz, Ar-H), 7.44 (d, 2H, J = 8.9 Hz, Ar-H), 7.32 (t, 1H, J = 7.1 Hz, Ar-H), 6.89 (t, 1H, J = 7.1 Hz, Ar-H), 6.64 (d, 1H, J = 7.1 Hz, Ar-H), 5.85 (s, 1H, -NH-CH-NH), 5.75 (s, 1H, -NH-CO), 4.32 (s, 1H, -NH-CH-NH). ¹³C NMR (50 MHz, CDCl₃, δ, ppm): 163.10 (1C, Ar-CO), 146.46 (1C, Ar-C), 139.06 (1C, Ar-C), 133.14 (1C, Ar-C), 132.23 (1C, Ar-C), 130.38 (1C, Ar-C), 130.10 (1C, Ar-C), 128.32 (1C, Ar-C), 127.78 (1C, Ar-C), 126.39 (1C, Ar-C), 121.07 (1C, Ar-C), 116.52 (1C, Ar-C), 113.73 (1C, Ar-C), 65.61 (1C, NH-CH-NH). MS (EI, m/z (%)): 303 [M⁺, 100].

2-(4-Hydroxyphenyl)-2,3-dihydroquinazolin-4(1H)-one (Entry 7): Color: White. Yield: 85%. M.p.: 278-280 °C. FT-IR (KBr, ν, cm⁻¹): 3305 (NH), 3189 (NH), 3061 (CH) (NH-CH-NH), 2928 (C=C-H), 1659 (C=O) 1607 (CONH), 1533 (C=C), 1461 (C=C), 1345 (C=C). ¹H NMR (300 MHz, CDCl₃, δ, ppm): 9.34 (s, 1H, br, Ar-H), 7.76 (d, J = 7.7 Hz, 1H, Ar-H), 7.38 (d, J = 7.1 Hz, 3H, Ar-H), 7.23 (t, J = 7.3 Hz, 1H, Ar-H), 6.84-6.68 (m, 4H, Ar-H), 6.29 (s, 1H, -CO-NH-CH-NH), 5.73 (s, 1H, -NH-CH-NH). ¹³C NMR (50 MHz, CDCl₃, δ, ppm): 160.99 (1C, Ar-CO), 156.33 (1C, Ar-C), 146.67 (2C, Ar-C), 132.72 (2C, Ar-C), 128.08 (3C, Ar-C), 118.91

(2C, Ar-C), 115.66 (1C, Ar-C), 113.90 (1C, Ar-C), 65.60 (1C, NH-CH-NH). MS (EI, m/z (%)): 241 [M^+ , 100].

2-(*p*-Tolyl)-2,3-dihydroquinazolin-4(1H)-one (Entry 8): Color: White. Yield: 86%. M.p.: 223-225 °C. FT-IR (KBr, ν , cm^{-1}): 3310 (NH), 3192 (NH), 3060 (CH) (NH-CH-NH), 2924 (C=C-H), 1662 (C=O) 1607 (CONH), 1509 (C=C), 1461 (C=C), 1345 (C=C). ^1H NMR (300 MHz, CDCl_3 , δ , ppm): 7.94 (d, $J = 7.2$ Hz, 1H, Ar-H), 7.45 (d, $J = 8.3$ Hz, 2H, Ar-H), 7.35-7.24 (m, 3H, Ar-H), 6.90 (t, $J = 7.2$ Hz, 1H, Ar-H), 6.66 (d, $J = 7.2$ Hz, 1H, Ar-H), 5.87 (s, 1H, Ar-H), 5.77 (s, 1H, NH-CO), 4.35 (s, 1H, NH-CH), 2.40 (s, 3H, Ar- CH_3). ^{13}C NMR (50 MHz, CDCl_3 , δ , ppm): 167.16 (1C, Ar-CO), 133.98 (3C, Ar-C), 129.74 (2C, Ar-C), 128.68 (2C, Ar-C), 127.28 (2C, Ar-C), 119.62 (2C, Ar-C), 114.54 (1C, Ar-C), 68.85 (1C, NH-CH-NH), 29.56 (1C, Ar- CH_3). MS (EI, m/z (%)): 239 [M^+ , 100].

2-(2-Methoxyphenyl)-2,3-dihydroquinazolin-4(1H)-one (Entry 9): Color: White. Yield: 87%. M.p.: 184-186 °C. FT-IR (KBr, ν , cm^{-1}): 3448 (NH), 3315 (NH), 3183 (CH) (NH-CH-NH), 2923 (C=C-H), 1676 (C=O) 1599 (CONH), 1473 (C=C), 1345 (C=C). ^1H NMR (300 MHz, CDCl_3 , δ , ppm): 8.56-8.53 (m, 1H, Ar-H), 8.33-8.29 (m, 1H, Ar-H), 7.81-7.74 (m, 1H, Ar-H), 7.56-7.41 (m, 2H, Ar-H), 7.18 (t, $J = 6.7$ Hz, 1H, Ar-H), 7.07 (d, $J = 6.7$ Hz, 1H, Ar-H), 6.91-6.87 (m, 1H, Ar-H), 6.66-6.62 (m, 1H, Ar-H), 6.56 (t, $J = 6.7$ Hz, 1H, Ar-H), 4.43 (s, 1H, NH-CH), 4.06 (s, 3H, O- CH_3). ^{13}C NMR (50 MHz, CDCl_3 , δ , ppm): 170.55 (1C, Ar-CO), 155.93 (1C, Ar-C), 148.33 (1C, Ar-C), 132.68 (1C, Ar-C), 131.05 (1C, Ar-C), 129.24 (1C, Ar-C), 127.60 (1C, Ar-C), 126.46 (1C, Ar-C), 125.90 (1C, Ar-C), 124.76 (1C, Ar-C), 124.38 (1C, Ar-C), 119.35 (1C, Ar-C), 118.65 (1C, Ar-C), 70.34 (1C, NH-CH-NH-), 54.38 (1C, Ar-O- CH_3). MS (EI, m/z (%)): 255 [M^+ , 100].

2-(4-Allyloxyphenyl)-2,3-dihydroquinazolin-4(1H)-one (Entry 10): Color: White. Yield: 84%. M.p.: 220-222 °C. FT-IR (KBr, ν , cm^{-1}): 3299 (NH), 3187 (NH), 3061 (CH) (NH-CH-NH), 2922 (C=C-H), 1651 (C=O) 1611 (CONH), 1509 (C=C), 1484 (C=C). ^1H NMR (300 MHz, CDCl_3 , δ , ppm): 7.94 (d, $J = 6.8$ Hz, 1H, Ar-H), 7.48 (d, $J = 8.0$ Hz, 2H, Ar-H), 7.33 (t, $J = 8.0$ Hz, 1H, Ar-H), 6.96 (d, $J = 8.0$ Hz, 2H, Ar-H), 6.88 (t, $J = 8.0$ Hz, 1H, Ar-H), 6.66 (d, $J = 8.0$ Hz, 1H, Ar-H), 6.08-6.00 (m, 1H, Ar-H), 5.85 (s, 1H, NH-CH-NH), 5.72 (s, 1H, NH-CO), 5.41 (d, $J = 17.1$ Hz, 1H, -C=C-H), 5.31 (d, $J = 9.1$ Hz, 1H, C=C-H), 4.56 (d, $J = 5.7$ Hz, 2H, O- CH_2), 4.34 (s, 1H, NH-CH). ^{13}C NMR (50 MHz, CDCl_3 , δ , ppm): 161.91 (1C, Ar-CO), 147.35 (1C, Ar-C), 133.97 (1C, O- CH_2 -CH=CH $_2$), 132.86 (1C, Ar-C), 131.75 (1C, Ar-C), 129.15 (1C, Ar-C), 127.85 (1C, Ar-C), 127.16 (1C, Ar-C), 125.74 (1C, Ar-C), 125.48 (1C, Ar-C), 119.72 (1C, Ar-C), 117.22 (1C, Ar-C), 116.87 (1C, O- CH_2 -CH=CH $_2$), 114.13 (1C, Ar-H), 113.90 (1C, Ar-H), 68.04 (1C, NH-CH-NH), 67.87 (1C, -O- CH_2). MS (EI, m/z (%)): 281 [M^+ , 100].

2-(2,5-Dimethylphenyl)-2,3-dihydroquinazolin-4(1H)-one (Entry 11): Color: White. Yield: 85%. M.p.: 223-225 °C. FT-IR (KBr, ν , cm^{-1}): 3312 (NH), 3192 (NH), 3061 (CH) (NH-CH-NH), 2924 (C=C-H), 1662 (C=O) 1607 (CONH), 1509 (C=C). ^1H NMR (300 MHz, CDCl_3 , δ , ppm): 7.88 (d, $J = 6.9$ Hz, 1H, Ar-H), 7.51 (s, 1H, Ar-H), 7.31 (t, $J = 6.9$ Hz, 1H, Ar-H), 7.07 (s, 3H, Ar-H), 6.86 (t, $J = 6.9$ Hz, 1H, Ar-H), 6.68 (d, $J = 7.9$ Hz, 1H, Ar-H), 6.21 (s, 1H, NH-CO), 6.08 (s, 1H, NH-CH-NH), 2.38 (s, 3H, Ar- CH_3), 2.31 (s, 3H, Ar- CH_3). ^{13}C NMR (50 MHz, CDCl_3 , δ , ppm): 163.18 (1C, Ar-CO), 147.13 (1C, Ar-C), 135.71 (1C, Ar-C), 133.43 (1C, Ar-C), 131.61 (1C, Ar-C), 129.06 (1C, Ar-C), 127.66 (1C, Ar-C), 126.68 (1C, Ar-C), 126.01 (1C, Ar-C), 125.15 (1C, Ar-C), 124.64 (1C, Ar-C), 115.85 (1C, Ar-C), 113.35 (1C, Ar-C), 63.56 (1C, NH-CH-NH), 19.25 (1C, Ar- CH_3), 16.85 (1C, Ar- CH_3). MS (EI, m/z (%)): 253 [M^+ , 100].

2-(3,4-Dihydroxyphenyl)-2,3-dihydroquinazolin-4(1H)-one (Entry 12): Color: White. Yield: 84%. M.p.: 290-292 °C. FT-IR (KBr, ν , cm^{-1}): 3313 (NH), 3193 (NH), 3062 (CH) (NH-CH-NH), 2925 (C=C-H), 1663 (C=O), 1608 (CONH), 1510 (C=C). ^1H NMR (300 MHz, CDCl_3 , δ , ppm): 8.84 (s, 1H, br, Ar-H), 7.80-7.57 (m, 2H, Ar-H), 7.41 (t, $J = 7.5$ Hz, 1H, Ar-H), 7.21 (t, $J = 7.1$ Hz, 1H, Ar-H), 7.04 (s, 1H, Ar-H), 6.89 (d, $J = 8.3$ Hz, 1H, Ar-H), 6.80-6.66 (m, 2H, Ar-H), 5.65 (s, 1H, CH-NH), 3.59 (s, 2H, Ar-OH). ^{13}C NMR

(50 MHz, CDCl_3 , δ , ppm): 162.67 (1C, Ar-CO), 150.88 (1C, Ar-C-OH), 147.85 (1C, Ar-C-OH), 147.44 (1C, Ar-C), 146.85 (1C, Ar-C), 146.28 (1C, Ar-C), 143.96 (1C, Ar-C), 143.65 (1C, Ar-C), 143.37 (1C, Ar-C), 132.98 (1C, Ar-C), 130.58 (1C, Ar-C), 125.77 (1C, Ar-C), 118.24 (1C, Ar-C), 64.98 (1C, NH-CH-NH). MS (EI, m/z (%)): 257 [M^+ , 100].

2-(1H-Indol-3-yl)-2,3-dihydroquinazolin-4(1H)-one (Entry 13): Color: White. Yield: 80%. M.p.: 232-235 °C. FT-IR (KBr, ν , cm^{-1}): 3311 (NH), 3191 (NH), 3060 (CH) (NH-CH-NH), 2923 (C=C-H), 1661 (C=O), 1606 (CONH), 1508 (C=C). ^1H NMR (300 MHz, CDCl_3 , δ , ppm): 10.08 (s, 1H, Ar-H), 8.92 (s, 1H, Ar-H), 8.34-8.30 (m, 3H, Ar-H), 7.85 (d, $J = 3.0$ Hz, 2H, Ar-H), 7.44 (t, $J = 5.1$ Hz, 2H, Ar-H), 7.35-7.30 (m, 2H, Ar-H), 5.81 (s, 1H, CH-NH), 4.94 (s, 1H, NH-Ar). ^{13}C NMR (50 MHz, CDCl_3 , δ , ppm): 161.43 (1C, Ar-CO), 151.71 (1C, Ar-C), 136.02 (2C, Ar-C), 133.74 (2C, Ar-C), 131.83 (1C, Ar-C), 131.28 (1C, Ar-C), 128.14 (2C, Ar-C), 127.13 (1C, Ar-C), 126.22 (2C, Ar-C), 115.96 (2C, Ar-C), 67.74 (1C, NH-CH-NH). MS (EI, m/z (%)): 264 [M^+ , 100].

2-(Thiophen-2-yl)-2,3-dihydroquinazolin-4(1H)-one (Entry 14): Color: White. Yield: 81%. M.p.: 211-213 °C. FT-IR (KBr, ν , cm^{-1}): 3448 (NH), 2923 (NH), 2853 (CH) (NH-CH-NH), 1763 (C=O), 1651 (CONH), 1457 (C=C), 1376 (C=C). ^1H NMR (300 MHz, CDCl_3 , δ , ppm): 7.93 (d, $J = 7.5$ Hz, 1H, Ar-H), 7.41-7.32 (m, 2H, Ar-H), 7.22 (d, $J = 3.7$ Hz, 1H, Ar-H), 7.02 (t, $J = 4.5$ Hz, 1H, Ar-H), 6.92 (t, $J = 7.5$ Hz, 1H, Ar-H), 6.70 (d, $J = 8.3$ Hz, 1H, Ar-H), 6.20 (s, 1H, NH-CH-NH), 6.13 (s, 1H, NH-CO), 4.56 (s, 1H, NH-CH). ^{13}C NMR (50 MHz, CDCl_3 , δ , ppm): 161.95 (1C, Ar-CO), 132.33 (1C, Ar-C), 126.49 (1C, Ar-C), 125.26 (1C, Ar-C), 124.89 (2C, Ar-C), 124.76 (1C, Ar-C), 116.93 (2C, Ar-C), 113.72 (1C, Ar-C), 102.96 (1C, Ar-C), 62.28 (1C, NH-CH-NH). MS (EI, m/z (%)): 231 [M^+ , 100]. Anal. calcd. for ($\text{C}_{12}\text{H}_{10}\text{N}_2\text{OS}$): C, 62.59; H, 4.38; N, 12.16. Found: C, 62.51; H, 4.24; N, 12.12%.

2-(1H-Pyrrol-2-yl)-2,3-dihydroquinazolin-4(1H)-one (Entry 15): Color: White. Yield: 82%. M.p.: 160-162 °C. FT-IR (KBr, ν , cm^{-1}): 3293 (NH), 3190 (NH), 3072 (CH) (NH-CH-NH), 2923 (C=C-H), 1654 (C=O), 1608 (CONH), 1533 (C=C). ^1H NMR (300 MHz, CDCl_3 , δ , ppm): 8.33-8.23 (m, 1H, Ar-H), 8.12 (s, 2H, Ar-H), 7.91-7.75 (m, 1H, Ar-H), 7.56-7.46 (m, 2H, Ar-H), 7.35 (d, $J = 1.5$ Hz, 1H, Ar-H), 6.88 (t, $J = 7.5$ Hz, 1H, Ar-H), 6.78 (s, 1H, NH-CO-Ar), 6.66 (s, 1H, NH-CH-NH), 5.09 (s, 1H, NH-CH-Ar). ^{13}C NMR (50 MHz, CDCl_3 , δ , ppm): 160.52 (1C, Ar-CO), 151.88 (1C, Ar-C), 147.34 (1C, Ar-C), 143.65 (1C, Ar-C), 132.91 (2C, Ar-C), 125.86 (1C, Ar-C), 125.46 (2C, Ar-C), 124.78 (2C, Ar-C), 62.54 (1C, NH-CH-NH). MS (EI, m/z (%)): 214 [M^+ , 100].

2-(Pyridin-4-yl)-2,3-dihydroquinazolin-4(1H)-one (Entry 16): Color: White. Yield: 82%. M.p.: 184-186 °C. FT-IR (KBr, ν , cm^{-1}): 3290 (NH), 3190 (NH), 3071 (CH) (NH-CH-NH), 2925 (C=C-H), 1652 (C=O), 1604 (CONH), 1535 (C=C), 1461 (C=C). ^1H NMR (300 MHz, CDCl_3 , δ , ppm): 8.90 (d, $J = 6.0$ Hz, 2H, Ar-H), 8.37 (d, $J = 7.5$ Hz, 2H, Ar-H), 8.17 (d, $J = 4.5$ Hz, 2H, Ar-H), 7.87 (d, $J = 3.0$ Hz, 2H, Ar-H), 7.62-7.57 (m, 1H, Ar-H), 5.80 (s, 1H, NH-CH-NH), 5.01 (s, 1H, NH-Ar). ^{13}C NMR (50 MHz, CDCl_3 , δ , ppm): 160.94 (1C, Ar-CO), 147.98 (1C, Ar-C), 146.87 (1C, Ar-C), 132.95 (2C, Ar-C), 126.33 (2C, Ar-C), 125.84 (1C, Ar-C), 124.46 (2C, Ar-C), 120.20 (2C, Ar-C), 69.15 (1C, NH-CH-NH). MS (EI, m/z (%)): 226 [M^+ , 100].

2-Phenethyl-2,3-dihydroquinazolin-4(1H)-one (Entry 17): Color: White. Yield: 79%. M.p.: 210-212 °C. FT-IR (KBr, ν , cm^{-1}): 3293 (NH), 3190 (NH), 3072 (CH) (NH-CH-NH), 2922 (C=C-H), 1695 (C=O), 1603 (CONH), 1533 (C=C). ^1H NMR (300 MHz, CDCl_3 , δ , ppm): 7.86 (d, $J = 8.1$ Hz, 1H, Ar-H), 7.38-7.22 (m, 4H, Ar-H), 6.84 (t, $J = 7.2$ Hz, 1H, Ar-H), 6.67-6.53 (m, 3H, Ar-H), 5.76 (s, 1H, NH-CO), 4.90 (t, $J = 5.4$ Hz, 1H, CH- CH_2), 4.11 (s, 1H, NH-CH-NH), 2.88-2.74 (m, 2H, CH $_2$ -CH $_2$ -Ar), 2.13-2.09 (q, $J = 7.2$ Hz, 2H, -CH-CH $_2$ -CH $_2$ -Ar). ^{13}C NMR (50 MHz, CDCl_3 , δ , ppm): 170.32 (1C, Ar-CO), 147.72 (1C, Ar-C), 140.01 (1C, Ar-C), 132.83 (1C, Ar-C), 131.85 (1C, Ar-C), 130.74 (1C, Ar-C), 127.42 (1C, Ar-C), 126.91 (1C, Ar-C), 124.41 (1C, Ar-C), 116.05 (1C, Ar-C), 115.77 (1C, Ar-C), 113.78 (1C, Ar-C), 113.22 (1C, Ar-C),

63.01 (1C, NH-CH-NH), 35.59 (1C, Ar-CH₂-CH₂), 27.98 (1C, Ar-CH₂-CH₂). MS (EI, *m/z* (%)): 253 [M⁺, 100].

(*E*)-2-Styryl-2,3-dihydroquinazolin-4(1*H*)-one (Entry 18): Color: White. Yield: 78%. M.p.: 209-211 °C. FT-IR (KBr, ν , cm⁻¹): 3296 (NH), 3191 (NH), 3071 (CH) (NH-CH-NH), 2925 (C=C-H), 1658 (C=O), 1610 (CONH). ¹H NMR (300 MHz, CDCl₃, δ , ppm): 7.88 (d, *J* = 8.2 Hz, 1H, Ar-H), 7.41-7.31 (m, 6H, Ar-H), 6.87 (t, *J* = 7.1 Hz, 1H, Ar-H), 6.72-6.65 (m, 3H, Ar-H), 6.36-6.32 (q, *J* = 16.4 Hz, 1H, NH-CH-NH), 5.45 (d, *J* = 8.2 Hz, 1H, CH=CH-Ar), 4.37 (s, 1H, NH-CH). ¹³C NMR (50 MHz, CDCl₃, δ , ppm): 160.46 (1C, Ar-CO), 149.85 (1C, Ar-C), 147.98 (1C, Ar-C), 147.28 (1C, Ar-C), 146.96 (1C, Ar-C), 138.92 (1C, Ar-C), 136.88 (1C, Ar-C), 132.40 (1C, Ar-C), 127.20 (1C, Ar-C), 126.64 (1C, Ar-C), 125.93 (1C, Ar-C), 124.38 (1C, Ar-C), 124.21 (1C, Ar-C), 124.12 (1C, NH-CH-CH=CH-Ar), 119.25 (1C, NH-CH-CH=CH-Ar), 63.01 (1C, NH-CH-NH). MS (EI, *m/z* (%)): 251 [M⁺, 100].

3. Results and discussion

In continuation of our efforts toward the development of novel environmentally benign/eco-friendly methodologies which include the synthesis of heterocyclic compounds, herein, we report a mild and efficient one-pot protocol for the synthesis of 2-phenyl-2,3-dihydroquinazolin-4(1*H*)-one derivatives for the first time by a two-component reaction involving anthranilamide, and aldehyde using a PEG-400 as a recyclable reaction medium (Scheme 1). In our initial studies toward the development of this methodology, anthranilamide (1.0 mmol) was reacted with aldehyde (1.0 mmol) in PEG-400 at room temperature yielding the corresponding 2-phenyl-2,3-dihydroquinazolin-4(1*H*)-one in 48% yield after 5 h. When the same reaction was attempted in PEG-400 at 100-110 °C the reaction proceeded to completion within 10 h and yielded the corresponding 2-phenyl 2,3-dihydroquinazolin-4(1*H*)-one in 85 % yield (Table 1). In all these reactions PEG-400 can be recovered and reused. Several examples illustrating this simple and practical methodology are summarized in Table 1. All the products were characterized by ¹H, ¹³C NMR, IR, and mass spectra and compared with the authentic samples [15].

Table 1. Synthesis of 2-phenyl-2,3-dihydroquinazolin-4(1*H*)-one derivatives.^a

Entry	Aldehyde	Product	Yield (%) ^b
1			85
2			85
3			92
4			88
5			88
6			89
7			85

^a Reaction conditions: aromatic aldehyde (1.0 mmol), anthranilamide (1.0 mmol), PEG-400 (5 mL), 100-110 °C, 4-10 h.

^b Isolated yield.

Table 1. (Continued).

Entry	Aldehyde	Product	Yield (%) ^b
8			86
9			87
10			84
11			85
12			84
13			80
14			81
15			82
16			82
17			79
18			78

^a Reaction conditions: aromatic aldehyde (1.0 mmol), anthranilamide (1.0 mmol), PEG-400 (5 mL), 100-110 °C, 4-10 h.

^b Isolated yield.

4. Conclusion

In summary, we have described a simple, efficient, and eco-friendly protocol for the synthesis of 2-phenyl-2,3-dihydroquinazolin-4(1*H*)-one derivatives in excellent yields under neutral conditions in one-pot catalyzed by recyclable PEG-400.

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References

- Mannschreck, A.; Koller, H.; Stuhler, G.; Davies, M. A.; Traber, J. E. *J. Med. Chem.* **1994**, *19*, 381-383.
- Russel, H. E.; Alaimo, R. J. *J. Med. Chem.* **1972**, *15*, 335-336.
- Dabiri, M.; Salehi, P.; Otokesh, S.; Baghbanzadeh, M.; Kozehgary, G.; Mohammadi, A. A. *Tetrahedron Lett.* **2005**, *46*, 6123-6126.
- Rostamizadeh, S.; Amani, A. M.; Aryan, R.; Ghaieni, H. R.; Shadjou, N. *Synth. Commun.* **2008**, *38*, 3567-3576.
- Dabiri, M.; Salehi, P.; Baghbanzadeh, M. *Monatsh. Chem.* **2007**, *138*, 1191-1194.
- Salehi, P.; Dabiri, M.; Baghbanzadeh, M.; Bahramnejad, M. *Synth. Commun.* **2006**, *36*, 2287-2292.
- Chen, J. X.; Wu, D. Z.; He, F.; Liu, M. C.; Wu, H. Y.; Ding, J. C.; Su, W. K. *Tetrahedron Lett.* **2008**, *49*, 3814-3818.

- [8]. Rostamizadeh, S.; Amani, A. M.; Mahdavinia, G. H.; Sepehrian, H.; Ebrahimi, S. *Synthesis* **2010**, 1356-1360.
- [9]. Dabiri, M.; Salehi, P.; Baghbanzadeh, M.; Zolfigol, M. A.; Agheb, M.; Heydari, S. *Catal. Commun.* **2008**, *9*, 785-788.
- [10]. Shaterian, H. R.; Oveisi, A. R.; Honarmand, M. *Synth. Commun.* **2010**, *40*, 1231-1242.
- [11]. Wang, L. M.; Hu, L.; Shao, J. H.; Yu, J. J.; Zhang, L. *J. Fluorine Chem.* **2008**, *129*, 1139-1145.
- [12]. Wang, M.; Zhang, T. T.; Song, Z. G. *Chin. Chem. Lett.* **2011**, *22*, 427-430.
- [13]. Kumari, K.; Raghuvanshi, D. S.; Singh, K. N. *India J. Chem. B* **2012**, *51*, 860-865.
- [14]. Jaber, Z. K.; Arjmandi, R. *Monatsh Chem.* **2011**, *142*, 631-635.
- [15]. Ramesh, K.; Karnakar, K.; Satish, G.; Kumar, B. S. P. A.; Nageswar, Y. V. D. *Tetrahedron Lett.* **2012**, *53*, 6936-6939.
- [16]. Johar, M.; Manning, T.; Kunimoto, D. Y.; Kumar, R. *Bioorg. Med. Chem.* **2005**, *13*, 6663-6671.
- [17]. Haimov, A.; Neumann, R. *Chem. Commun.* **2002**, 876-877.
- [18]. Blanton, J. R. *Synth. Commun.* **1997**, *27*, 2093-2102.
- [19]. Chandrasekhar, S.; Narsihmulu, C.; Sultana, S. S.; Reddy, N. R. K. *Org. Lett.* **2002**, *4*, 4399-4401.
- [20]. Ferraboschi, P.; Fiecchi, A.; Grisenti, P.; Santaniello, E.; Trave, S. *Synth. Commun.* **1987**, *17*, 1569-1575.