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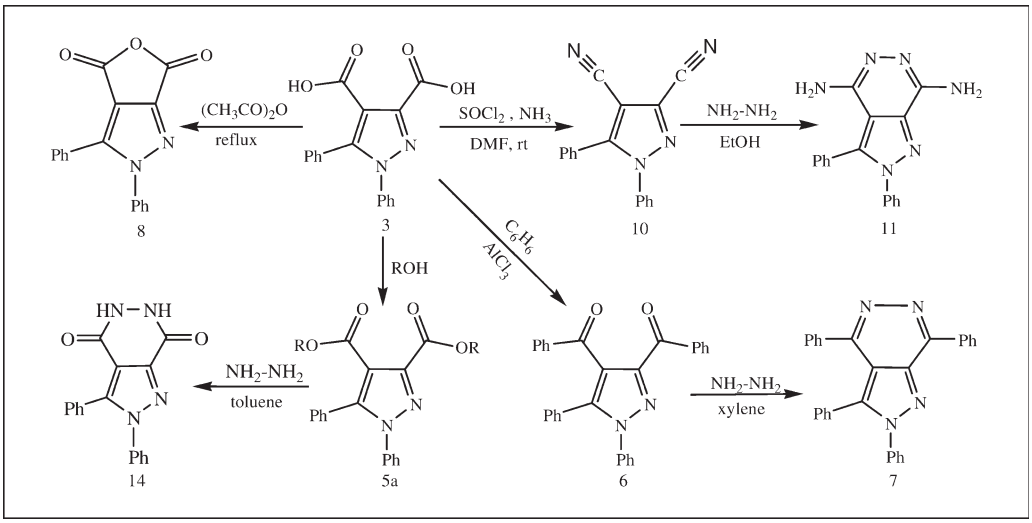

Compound of 4-(ethoxycarbonyl)-1,5-diphenyl-1*H*-pyrazole-3-carboxylic acid **2** was obtained from the reaction of ethyl 4,5-dioxo-2-phenyl-4,5-dihydrofuran-3-carboxylate and 1-benzylidene-2-phenylhydrazine. A number of substitute pyrazole dicarboxylic acid derivatives (**4, 5a–c, 6, 7, 8, 9a–m, 10, 11, 12, 13, 14**) were synthesized from 1,5-diphenyl-1*H*-pyrazole-3,4-dicarboxylic acid **3** which was prepared from basic hydrolysis of **2**. Structures of synthesized compounds were characterized by ^{1}H NMR, ^{13}C NMR, Mass, FTIR, and elemental analysis.

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INTRODUCTION

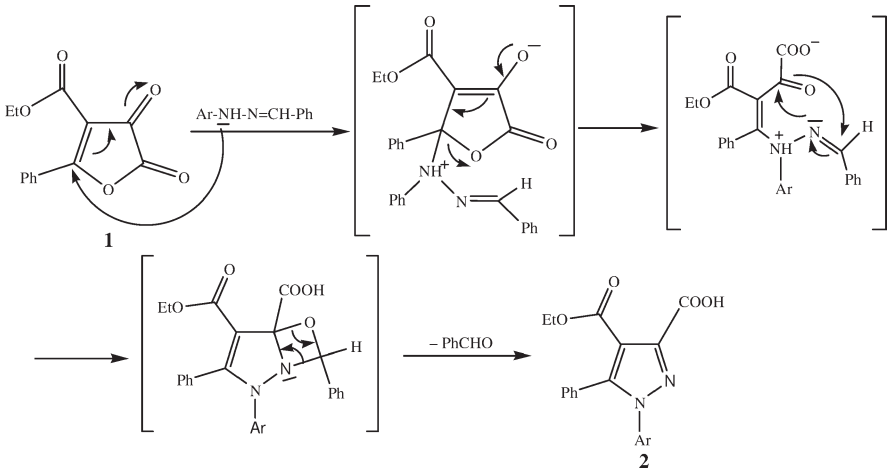
The chemistry of pyrazole derivatives have been the subject of much research because of their importance in various applications and their widespread potential biological and pharmacological activities such as antimicrobial, antiviral, antitumor, anti-inflammatory, pesticidal, antifungal, antidepressant, antipyretic, and analgesic [1–10]. Thus, these compounds have been the focus of high attention among medicinal chemists [11–16]. It is also known that biological activities of pyrazole derivatives which include substituted heteroaryl groups increase and that some pyrazolo-pyridazine compounds which include the same heteroaryl groups are used as a cure for many diseases [17–25].

Pyrazole-3-carboxylic acid derivatives in general are well-known nitrogen-containing heterocyclic compounds, and various procedures have been developed for their syntheses [26–31]. In the literature, there is not much research related to the reactions of derivatives of 1,5-diphenyl-1*H*-pyrazole-3,4-dicarboxylic acids although a number of new derivatives of pyrazoles some of which have bicyclic structure were synthesized [26–29]. In this research, we decided to extend our previous studies to satisfy this deficiency and to synthesize different derivatives of pyrazole compounds that show biological activity [20,21,26,29].

RESULTS AND DISCUSSION

1,5-Diphenyl-1*H*-pyrazole-3,4-dicarboxylic acid **3**, which was our initial compound, was prepared after various reaction steps. First, ethyl 4,5-dioxo–2-phenyl-4,5–dihydrofuran–3-carboxylate **1** compound was prepared from the reactions of ethyl 3-oxo-3-phenylpropanoate and oxalyl dichloride [32,33]. Keeping in mind that H-active nucleophiles attack the C-2, C-3, and C-4 positions of furandiones and it starts the reactions in which intermediate products were formed, NH group attacks to

Scheme 1

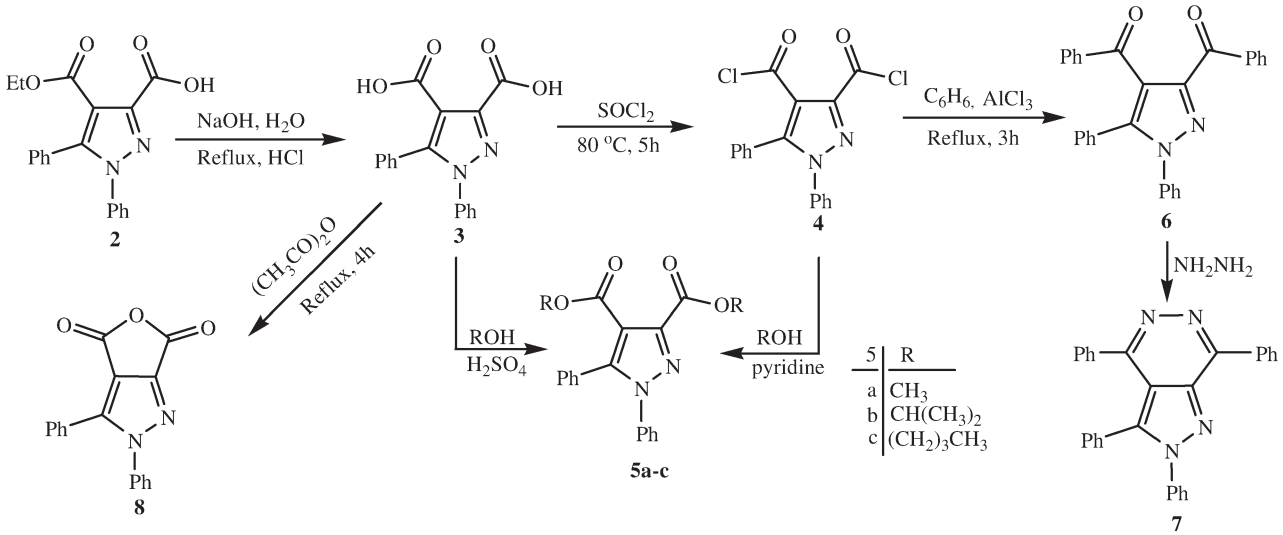


C-3 and C-4 positions of furandione in the condensation reaction of **1** with 1-benzylidene-2-phenylhydrazine in no solvent media [26,27,30]. The possible reaction steps of 4-(ethoxycarbonyl)-1,5-diphenyl-1H-pyrazole-3-carboxylic acid **2** was given in Scheme 1.

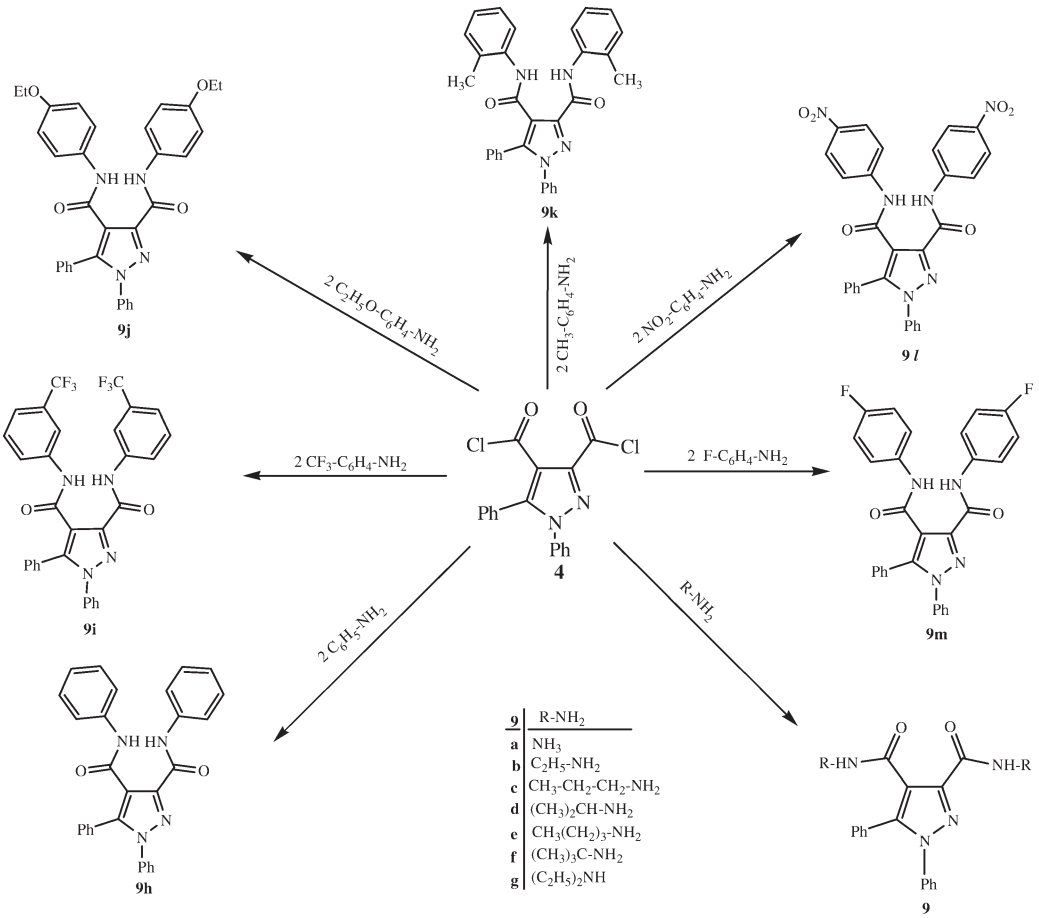
1,5-Diphenyl-1*H*-pyrazole-3,4-dicarboxylic acid **3** compound was prepared from the basic hydrolysis of **2** at a high yield (92%). The long reaction time increased the yield. The structure was confirmed with the characteristic IR absorption bands at 3354–2454 cm^{-1} (COOH), 3064 cm^{-1} (Ar CH), 1670 cm^{-1} (acid, C=O), 1597–1486 cm^{-1} (C=C and C=N) and the ^{13}C NMR signals at $\delta = 163.75$ and $\delta = 164.61$ (acid, C=O). 306 m/z (M-2) value in mass spectra for **3** showed the existence of molecular ion structure.

Diester derivatives of Compound **3** were obtained in two different methods. In the first method, carboxylic groups of **3** were activated with $SOCl_2$ and gave the **4**. Afterward, the diester derivatives **5a–c** were obtained from the reaction of **4** with various alcohols with pyridine catalyst. However, it was understood from TLC works that synthesized products by this method contained impurity. This impurity was probably resulted from pyridine and was difficult to remove. In the second method, compound **3** gave the purer diester products **5a–c** about in yield of 61–75%. For this reason, the compound **3** was heated with various alcohols in benzene with sulfuric acid catalyst (Scheme 2). The second method was chosen in this study. On the other hand, heating the compound **4** in dry benzene with $AlCl_3$

Scheme 2



Scheme 3



catalyst [34] gave 1-phenyl-1H-pyrazole-3,4-diyl) bis(phenylmethanone **6** (Scheme 2).

NH_2 groups of hydrazine which have strong nucleophilic property attacks to benzoyl carbons when the compound **6** was heated with anhydrous hydrazine. In the second stage, cyclization occurred with the removal of two moles water, and pyrazolo-pyridazine derivative **7** was obtained (Scheme 2).

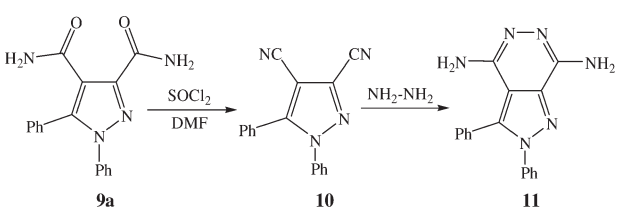
Moreover, heating of **3** in acetic anhydride caused the leaving of one mole water. As a result of this, furo[3,4-c] pyrazole-4,6-dione **8** (Scheme 2) was synthesized [35–37]. However, it was also observed from TLC controls that this compound was very sensitive to oxidation in air and returned to its initial compound. Therefore, it is suitable to handle this compound in desiccator by being dried with P_2O_5.

Derivatives of pyrazole-3,4-dicarboxamide **9a–m** were prepared easily by reaction of **4** with ammonia, substituted aryl amines, and a series of alkyl amines (Scheme 3). Structures of the compounds were confirmed with spectral data.

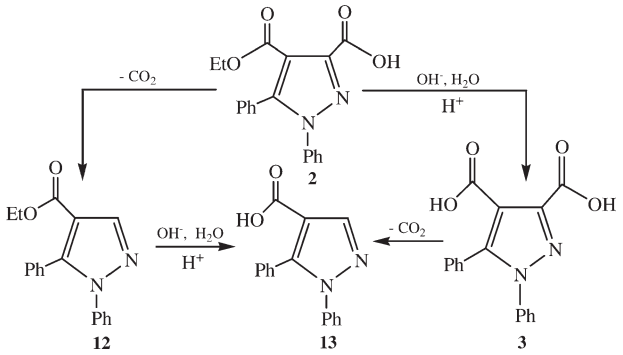
As a result of dehydration of **9a** in cold DMF and $SOCl_2$ mix, dinitrile **10** compound occurred at 96% yield [20,26]. Compound **10** showed characteristic IR absorption band at 2231 cm^{-1} (C≡N). IR spectra of compound **10** showed no absorption bands corresponding to the COOH group such as 3300–2500 cm^{-1} (COOH) and 1700–1750 cm^{-1} (acid, C=O) like the 1,5-diphenyl-1*H*-pyrazole-3,4-dicarboxylic acid. Furthermore, ^{13}C NMR signals at δ = 110.77–110.80 ppm were related to carbon of nitrile (C≡N).

Reaction of **10** with anhydrous hydrazine in absolute ethanol led to the formation of the 2,3-diphenyl-2H-pyrazolo[3,4-d]pyridazine-4,7-diamine **11** in about 69% yield (Scheme 4). Structure of the compound was confirmed with spectral data (See Experiments).

Scheme 4



Scheme 5



As a result of decarboxylation of **2** at high temperature (200–220°C), the compound **12** was obtained and the compound **13** was synthesized after basic hydrolysis of **12**. It was understood from TLC and spectral data that basic hydrolysis of **12** and decarboxylation of **3** gave the same products 1,5-diphenyl-1*H*-pyrazole-4-carboxylic acid **13**. After decarboxylation of **3**, it was shown that leaving carboxyl group bonded the adjacent carbon to nitrogen (Scheme 5).

On the other hand, cyclo-condensation reaction of **2** and **5a** with hydrazine hydrate gave the same product pyrazolo[3,4-d]pyridazine-4,7-dione **14** [6,26]. IR, ^{1}H NMR, and ^{13}C NMR spectra [IR: 3158–2629), ^{1}H NMR: 10.40 (br. s, 1H, NH—C=O), 5.30 (br. s, 1H, N=C—OH), ^{13}C NMR: 161.79 and 161.58 (C=O, C-4), 156.58 and 152.33 (C=O, C-7)] showed evidence of the presence of a tautomeric equilibrium (HN—C=O↔N=C—OH) between the two tautomers (keto-enol) of compound **14** (Scheme 6).

In this research, a number of derivatives of substituted pyrazole dicarboxylic acids were gained to pyrazole chemistry and characterization of each compound were performed with the help of spectral data (See Experiments).

EXPERIMENTS

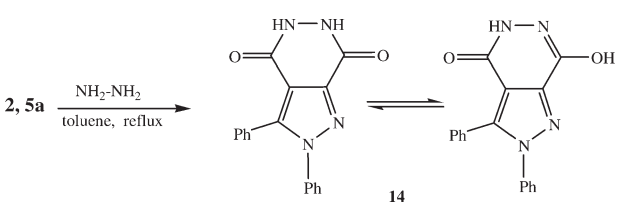
The optimum reaction conditions were determined considering the time, concentration, solvent, and structure of reactive compounds which were effective on yield and velocity of chemical reactions. Chemical compounds used in this research were at analytical purity, and the solvents were purified by using appropriate purifying agents and distillation. At the end of the each experiment, TLC was performed using DC Alufolien Kiesegel 60F/254 Merck and Camag TLC devices. Melting points were measured with Barnstead Electrothermal 9200 apparatus and were not corrected. IR spectrum data of compounds were determined by Mattson 1000 FTIR with using of KBr pellets. ^{1}H NMR and ^{13}C NMR spectra were evaluated by BRUKER DPX-400, (400MHz), and High Performance Digital FT-NMR (100MHz) spectrometers. Mass spectra data were determined by Varian Mat III 80 eV. Elemental analyses were carried out on a Leco CHNS-932 instrument.

1,5-Diphenyl-1*H*-pyrazole-3,4-dicarboxylic acid (3). Compound **2** of 0.336 g (1 mmol) was refluxed in solution of 0.1 g (2.5 mmol) NaOH for about 1.5 h. Mixed solution was cooled down to room temperature. It was stirred for a while by adding 1.5 mL concentrated HCl and water at equal volume. Precipitated white solid product was filtered and washed with water again. It was purified from water–ethanol mixture by crystallization. (283 mg, 92%); mp 224–225°C; IR (ν, cm^{-1}): 3354–2454 (OH, COOH), 3064 (CH, aromatic), 1670 (C=O), 1597–1486 (C=C and C=N); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.27–7.40 (m, 10H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 164.61 and 163.76 (C=O, acid), 144.85 (C–3), 144.31(C–5), 116.14 (C–4), 138.93, 130.53, 129.74, 129.52, 129.21, 128.67, 128.54, 126.32; MS(CI) m/z 306.0 (M–2, COO^-); Anal. Calcd. for $C_{17}H_{12}N_2O_4$: C, 66.23; H, 3.92; N, 9.09. Found: C, 66.56; H, 3.65; N, 9.12.

1,5-Diphenyl-1*H*-pyrazole-3,4-dicarbonyl dichloride (4). Compound **3** of 0.308 g (1 mmol) was refluxed with excessive $SOCl_2$ at 80°C for about 5 h. Excessive $SOCl_2$ was evaporated. Remaining oily product was purified in ether–hexane mixture. (259 mg, 75%); mp 86–89°C; IR (ν, cm^{-1}): 3060 (CH, aromatic), 1735 (C=O), 1620–1487 (C=C and C=N); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.00–7.72 (m, 10H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 161.39 and 161.09 (C=O), 146.54 (C–3), 143.96 (C–5), 120.35 (C-4), 137.82, 130.60, 130.09, 129.56, 129.35, 128.90, 126.13, 125.51; Anal. Calcd. for $C_{17}H_{10}Cl_2N_2O_2$: C, 59.15; H, 2.92; N, 8.12. Found: C, 59.35; H, 2.79; N, 8.10.

General procedure for compounds 5a–c. Compound **3 of** 1 mmol was dissolved in 10 mL dry benzene, and 2 mL alcohol (MeOH, *i*-PrOH, BuOH) and 0.2 mL H_2SO_4 was added to this solution. Mixture was refluxed for 4–5 h. After evaporation, some water was added to the product remaining at the bottom of the flask and transferred to separate funnel. 10 mL of ether was added

Scheme 6



to the mixture and was washed with 10% Na_2CO_3 solution. Ether was evaporated after separation of organic phase. The synthesized crude products **5a–c** were purified from hexane.

Dimethyl-1,5-diphenyl-1H-pyrazole-3,4-dicarboxylate (5a). (205 mg, 61%); mp 96–97°C; IR (ν, cm^{-1}): 3002 (CH, aromatic), 2952 (CH, aliphatic), 1718 (C=O), 1596–1497 (C=C and C=N); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.39–7.23 (m, 10H, ArH), 4.00 and 3.78 (s, 6H, $2OCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 163.48 and 162.31 (C=O), 144.86 (C–3), 143.21 (C–5), 115.56 (C–4), 52.63 and 52.25 ($2OCH_3$), 138.62, 130.05, 129.53, 128.99, 128.63, 128.38, 127.82, 125.63; Anal. Calcd. for $C_{19}H_{16}N_2O_4$: C, 67.85; H, 4.79; N, 8.33. Found: C, 67.68; H, 4.89; N, 8.32.

Diisopropyl-1,5-diphenyl-1H-pyrazole-3,4-dicarboxylate (5b). (239 mg, 61%); mp 96–97°C; IR (ν, cm^{-1}): 3059 (CH, aromatic), 2937 (CH, aliphatic), 1710 (C=O), 1599–1498 (C=C and C=N); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.39–7.24 (m, 10H, ArH), 5.36 and 5.12 (p, J = 6.3 Hz, 2H, 2OCH), 1.45 and 1.27 (d, J = 6.3 Hz, 12H, $2CH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 162.51 and 161.80 (C=O), 144.41 (C–3), 144.09 (C–2), 115.93 (C–4), 69.54 and 68.73 (OCH), 21.83 and 21.57 (CH_3), 138.73, 130.11, 129.32, 128.92, 128.44, 128.24, 128.22, 125.63; Anal. Calcd. for $C_{23}H_{24}N_2O_4$: C, 70.39; H, 6.16; N, 7.14. Found: C, 70.25; H, 6.19; N, 7.21.

Dibutyl 1,5-diphenyl-1H-pyrazole-3,4-dicarboxylate (5c). (286 mg, 68%); mp 49–50°C; IR (ν, cm^{-1}): 3062 (CH, aromatic), 2959 (CH, aliphatic), 1719 (C=O), 1596–1498 (C=C and C=N); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.38–7.23 (m, 10H, ArH), 4.42 and 4.18 (t, J = 6.8 Hz, 4H, $2OCH_2$), 1.81 (p, J = 7.2 Hz, 4H, $2OCH_2CH_2CH_2$), 1.62–1.46 (m, 4H, $CH_2CH_2CH_3$ and $OCH_2CH_2CH_2$), 1.21 (h, J = 7.5 Hz, 2H, $CH_2CH_2CH_3$), 0.99 and 0.86 (t, J = 7.4 Hz, 6H, $2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 163.03 and 162.31 (C=O), 144.64 (C–3), 143.94 (C–5), 115.49 (C–4), 65.60 and 64.99 (OCH_2), 30.65 and 30.41 ($CH_2CH_2CH_2$), 19.11 and 18.97 ($CH_2CH_2CH_3$), 13.75 and 13.64 (CH_3), 138.66, 130.10, 129.39, 128.92, 128.48, 128.31, 128.14, 125.58, 118.80; Anal. Calcd. for $C_{25}H_{28}N_2O_4$: C, 71.41; H, 6.71; N, 6.66. Found: C, 71.29; H, 6.79; N, 6.65.

(1,5-Diphenyl-1*H*-pyrazole-3,4-diyl)bis (phenylmethanone) (6). Compound **4** of 0.345 g (1 mmol) was dissolved in dry benzene, and 0.33 g (2.5 mmol) $AlCl_3$ was added to this solution. After cooling down of mixture which was refluxed for 3 h, organic phase was separated by adding some ether and ice water. Then ether was evaporated and the residue solid was recrystallized from ethanol–water mixture. (253 mg, 59%); mp 174–175°C; IR (ν, cm^{-1}): 3064 and 3028 (CH, aromatic), 1664 (C=O), 1617–1489 (C=C and C=N); ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.20–7.23 (m, 20H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 191.04 and 187.16 (C=O, benzoyl), 149.43 (C–3), 144.01 (C–5), 123.85 (C–4), 139.04, 137.98, 136.47, 134.01, 133.80, 130.72, 130.70, 130.29, 129.82, 129.64, 129.39, 129.05, 129.02, 128.90, 128.07, 126.48; Anal. Calcd. for $C_{29}H_{20}N_2O_2$: C, 81.29; H, 4.70; N, 6.54. Found: C, 81.42; H, 4.65; N, 6.51

2,3,4,7-Tetraphenyl-2*H*-pyrazolo[3,4-d]pyridazine (7). Compound **6** of 1 mmol was dissolved in dry xylene, and 0.1 mL hydrazine was added and refluxed for 4 h. Then, solvent was evaporated and 10 mL ether was added to residue product and stirred for a while in cold. Precipitated yellow product was filtered, washed with water, and purified from ethanol–water mixture by crystallization. (343 mg, 81%); mp 194–196°C; IR (ν, cm^{-1}): 3057 and 3030 (CH, aromatic), 1590–1488 (C=C and C=N); ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.57–7.01 (m, 20H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 156.57 and 149.93 (C–4 and C–7), 141.89, 139.85, 139.51, 137.01, 135.72, 135.35, 131.21, 130.80, 130.03, 129.53, 129.47, 129.41, 129.35, 129.13, 128.50, 128.32, 127.84, 127.28, 116.17 Anal. Calcd. for $C_{29}H_{20}N_4$: C, 82.05; H, 4.75; N, 13.20. Found: C, 81.93; H, 4.67; N, 13.28.

2,3-Diphenyl-2*H*-furo[3,4-c]pyrazole-4,6-dione (8). Compound **3 of** 0.308 g (1 mmol) was transferred to a flask. 2.5 mL acetic anhydride and 0.1 mL pyridine was added and refluxed for about 4 h. Excessive amount of solvent was evaporated. The residue product was purified from hexane and chloroform mixture by crystallization. (226 mg, 78%); mp 176–178°C; IR (ν, cm^{-1}): 3072 (CH, aromatic), 1810 and 1708 (C=O), 1628–1489 (C=C and C=N); ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.30–7.01 (m, 10H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 164.46 and 164.15 (C=O), 146.99, 140.71, 139.12, 130.77, 129.41, 129.23, 129.03, 128.43, 126.33, 125.74, 116.25; MS(CI) m/z 291.0 (M+1); Anal. Calcd. for $C_{17}H_{10}N_2O_3$: C, 70.34; H, 3.47; N, 9.65. Found: C, 70.48; H, 3.35; N, 9.72.

1,5-Diphenyl-1*H*-pyrazole-3,4-dicarboxamide (9a). Compound **4** of 0.345 g (1 mmol) was dissolved in CCl_4 and cooled down to 0°C. Excessive amount of NH_3 was added to this solution. To complete the reaction, mixture was stirred for about an hour at room temperature. Precipitated white product was washed with water and purified from ethanol by crystallization.

(217 mg, 71%); mp 286–287°C; IR (ν, cm^{-1}): 3308 and 3146 (NH), 3073 (CH, aromatic), 1650 (amide C=O), 1587–1489 (C=C and C=N); ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.06 and 7.76 (br. 4H, $2NH_2$), 7.39–7.24 (m, 10H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 165.10 and 161.30 (C=O), 143.60 (C–3),

139.56 (C–5), 119.80 (C–4), 130.15, 129.81, 129.55, 129.12, 128.40, 128.31, 128.13, 123.50; MS(CI) m/z 307.1 (M+1); Anal. Calcd. for $C_{17}H_{14}N_4O_2$: C, 66.66; H, 4.61; N, 18.29. Found: C, 66.61; H, 4.69; N, 18.27.

General procedure for compounds 9b–m. Compound **4** of 0.345 g (1 mmol) was dissolved in 10 mL dry xylene and 4 mmol aryl or alkyl amine compound was added. Mixture was refluxed for 3 h and solvent was evaporated. The crude product was washed with water and purified from an appropriate solvent.

1,5-Diphenyl-N³,N⁴-diethyl-1H-pyrazole-3,4-dicarboxamide (9b). (304 mg, 84%); mp 138–139°C; (was crystallized from EtOH/H_2O); IR (ν, cm^{-1}): 3456 and 3291 (NH), 3077 (CH, aromatic), 2974 and 2930 (CH, aliphatic), 1644 (C=O), 1553–1496 (C=C and C=N); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 10.35 (m, 2H, 2NH), 7.35–7.17 (m, 10H, ArH), 3.52 and 3.40 (p, J = 3.6 Hz, 4H, $2CH_2$), 1.32 and 1.21 (t, J = 7.3 Hz, 6H, $2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 163.15 and 161.36 (C=O), 148.38 (C–3), 142.56 (C–5), 117.34 (C–4), 34.49 and 34.08 ($NHCH_2$), 14.72 and 14.67 (CH_3), 138.78, 130.53, 129.85, 129.75, 128.85, 128.43, 127.95, 125.62; Anal. Calcd. for $C_{21}H_{22}N_4O_2$: C, 69.59; H, 6.12; N, 15.46. Found: C, 69.45; H, 6.21; N, 15.42.

1,5-Diphenyl-N³,N⁴-dipropyl-1H-pyrazole-3,4-dicarboxamide (9c). (320 mg, 82%); mp 135–136°C; (was crystallized from chloroform/hexane); IR (ν, cm^{-1}): 3361 and 3256 (NH), 3059 (CH, aromatic), 2962 and 2874 (CH, aliphatic), 1634 (C=O), 1555–1492 (C=C and C=N); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 10.37 (m, 2H, 2NH), 7.31–7.15 (m, 10H, ArH), 3.45 and 3.32 (q, J = 6.8 Hz, 4H, $2NHCH_2CH_2$), 1.69–1.59 (m, 4H, $2CH_2CH_2CH_3$), 0,94–1,02 (m, 6H, $2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 163.26 and 161.52 (C=O), 148.31 (C–3), 142.66 (C–5), 117.32 (C–4), 41.56 and 41.39 ($NHCH_2$), 22.89 and 22.85 (CH_2—CH_2), 11.73 and 11.55 (CH_3), 138.77, 130.53, 129.86, 128.84, 128.42, 128.11, 127.95, 125.61; Anal. Calcd. for $C_{23}H_{26}N_4O_2$: C, 70.75; H, 6.71; N, 14.35. Found: C, 70.63; H, 6.79; N, 14.32.

1,5-Diphenyl-N³,N⁴-diisopropyl-1H-pyrazole-3,4-dicarboxamide (9d). (332 mg, 85%); mp 159–160°C; (was crystallized from ether/hexane); IR (ν, cm^{-1}): 3389 and 3249 (NH), 3036 (CH, aromatic), 2967 and 2931 (CH, aliphatic), 1656 (C=O), 1633–1492 (C=C and C=N); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 10.21–10.19 (m, 2H, 2NH), 7.36–7.17 (m, 10H, ArH), 4.34 and 4.18 (m, 2H, $2NHCH(CH_3)_2$), 1.33 and 1.25 (d, J = 6.6 Hz, 12H, $4CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 162.35 and 160.61 (C=O), 148.27 (C–3), 142.76 (C–5), 117.57 (C–4), 41.59 and 40.99 (NHCH), 22.72 and 22.70 ($CH(CH_3)_2$), 138.81, 130.52, 129.91, 128.85, 128.82, 128.42, 127.96, 125.72; Anal. Calcd. for $C_{23}H_{26}N_4O_2$: C, 70.75; H, 6.71; N, 14.35. Found: C, 70.55; H, 6.82; N, 14.37.

1,5-Diphenyl-N³,N⁴-dibutyl-1H-pyrazole-3,4-dicarboxamide (9e). (334 mg, 80%); mp 133–134°C; (was crystallized from ether/hexane); IR (ν, cm^{-1}): 3371 and 3256 (NH), 3033 (CH, aromatic), 2960, 2931 and 2871 (CH, aliphatic), 1657 (C=O), 1627–1493 (C=C and C=N); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 10.34 and 7.51 (m, 2H, 2NH), 7.33–7.17 (m, 10H, ArH), 3.50 and 3.36 (q, J = 7.1 Hz, 4H, $2NHCH_2CH_2$), 1.65–1.59 (m, 4H, $2CH_2CH_2CH_2$), 1.54–1.22 (m, 4H, $2CH_2CH_3$), 1.11–0.78 (m, 6H, $2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 163.23 and 161.45 (C=O), 148.30 (C–3), 142.68 (C–5), 117.34 (C–4), 39.35 and 39.19 ($NHCH_2$), 31.55 ($CH_2CH_2CH_2$), 20.37 and 20.16 (CH_2CH_3), 13.89 and 13.32 (CH_3), 138.79, 130.54, 129.88, 128.84, 128.40, 128.38, 127.95, 125.61; Anal. Calcd. for $C_{25}H_{30}N_4O_2$: C, 71.74; H, 7.22; N, 13.39. Found: C, 71.59; H, 7.28; N, 13.45.

1,5-Diphenyl-N³,N⁴-di-tert-butyl-1H-pyrazole-3,4-dicarboxamide (9f). (343 mg, 82%); mp 174–175°C; (was crystallized from ether/hexane); IR (ν, cm^{-1}): 3393 and 3268 (NH), 3069 (CH, aromatic), 2968 and 2929 (CH, aliphatic), 1665 (C=O), 1643–1489 (C=C and C=N); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 9.44 and 7.39 (m, 2H, 2NH), 7.35–7.15 (m, 10H, ArH), 1.51 and 1.40 (s, 18H, $6CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 162.66 and 161.30 (C=O), 147.20 (C–3), 144.15 (C–5), 118.42 (C–4), 51.68 and 51.01 (NHC), 28.71 and 28.68 ($C(CH_3)_3$), 138.90, 130.40, 129.76, 128.92, 128.82, 128.28, 128.11, 125.74; Anal. Calcd. for $C_{25}H_{30}N_4O_2$: C, 71.74; H, 7.22; N, 13.39. Found: C, 71.59; H, 7.25; N, 13.38.

1,5-Diphenyl-N³,N³,N⁴,N⁴-tetraethyl-1H-pyrazole-3,4-dicarboxamide (9g). (322 mg, 77%); mp 134–135°C; (was crystallized from chloroform/hexane); IR (ν, cm^{-1}): 3063 (CH, aromatic), 2978 and 2940 (CH, aliphatic), 1656 (C=O), 1617–1496 (C=C and C=N); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.49–7.15 (m, 10H, ArH), 3.57 and 3.13 (q, J = 7.1 Hz, 8H, $4NCH_2$), 1.09 and 0.74 (t, J = 7.1 Hz, 12H, $4CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 164.46 and 162.68 (C=O), 145.63 (C–3), 139.42 (C–5), 119.97 (C–4), 43.49, 43.37, 40.31, 38.87 (NCH_2), 14.60, 13.36, 12.87, 12.44 (CH_3), 139.35, 131.53, 129.27, 128.91, 128.69, 128.54, 127.70, 125.02; Anal. Calcd. for $C_{25}H_{30}N_4O_2$: C, 71.74; H, 7.22; N, 13.39. Found: C, 71.65; H, 7.25; N, 13.41.

1,5,N³,N⁴,-Tetraphenyl-1H-pyrazole-3,4-dicarboxamide (9h). (357 mg, 78%); mp 209–210°C; (was crystallized from chloroform/hexane); IR (ν, cm^{-1}): 3465 (NH), 3030 (CH, aromatic), 1655 (C=O), 1599–1489 (C=C and C=N); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 12.54 and 9.45 (s, 2H, 2NH), 7.85–7.10 (m, 20H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 161.64 and 159.35 (C=O), 149.55 (C–3), 142.18 (C–5), 118.14 (C–4), 139.07, 138.58, 137.13, 130.62, 130.60, 129.50,

129.22, 129.00, 128.80, 128.78, 128.16, 125.76, 125.13, 123.70, 120.67, 120.33; Anal. Calcd. for $C_{29}H_{22}N_4O_2$: C, 75.97; H, 4.84; N, 12.22. Found: C, 75.86; H, 4.92; N, 12.19.

1,5-Diphenyl-N³,N⁴-bis(3-(trifluoromethyl) phenyl)-1H-pyrazole-3,4-dicarboxamide (9i). (434 mg, 73%); mp 202–203°C; (was crystallized from BuOH); IR (ν, cm^{-1}): 3464 and 3376 (NH), 3070 and 3023 (CH, aromatic), 1659 (C=O), 1626–1490 (C=C and C=N); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 12.61 and 9.48 (s, 2H, 2NH), 8.10–7.23 (m, 18H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 161.88 and 159.34 (C=O), 150.10 (C–3), 141.56 (C–5), 123.69 and 123.37 ($\underline{C}F_3$), 116.92 (C–4), 139.41, 138.35, 137.48, 130.49, 129.86, 129.43, 129.23, 129.07, 129.05, 129.01, 128.23, 125.73, 121.77, 121.74, 120.32, 120.28, 117.76, 117.32, 117.28, 116.96; Anal. Calcd. for $C_{31}H_{20}F_6N_4O_2$: C, 62.63; H, 3.39; N, 9.42. Found: C, 62.48; H, 3.45; N, 9.45.

1,5-Diphenyl-N³,N⁴-bis(4-ethoxyphenyl)-1H-pyrazole-3,4-dicarboxamide (9j). (410 mg, 75%); mp 210–211°C; (was crystallized from PhMe); IR (ν, cm^{-1}): 3459 and 3314 (NH), 3020 (CH, aromatic), 2857 (CH, aliphatic), 1665 (C=O), 1620–1501 (C=C and C=N); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 12.44 and 9.23 (s, 2H, 2NH), 7.74–6.83 (m, 18H, ArH), 4.27–3.86 (m, 4H, $2O\underline{C}H_2$), 1.39–1.47 (m, 6H, $2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 161.40 and 159.03 (C=O), 156.38 and 155.24 (C=C-OEt), 149.33 (C–3), 142.24 (C–5), 114.55 (C–4), 63.74 and 63.64 ($O\underline{C}H_2$), 14.89 (CH_3), 138.65, 132.23, 130.59, 129.95, 129.60, 129.11, 128.94, 128.68, 128.09, 125.73, 122.45, 121.77, 118.15, 114.91; Anal. Calcd. for $C_{33}H_{30}N_4O_4$: C, 72.51; H, 5.53; N, 10.25. Found: C, 72.45; H, 5.58; N, 10.24.

1,5-Diphenyl-N³,N⁴-di-o-tolyl-1H-pyrazole-3,4-dicarboxamide (9k). (365 mg, 75%); mp 195–196°C; (was crystallized from PhMe); IR (ν, cm^{-1}): 3489 and 3381 (NH), 3029 (CH, aromatic), 2922 and 2865 (CH, aliphatic), 1658 (C=O), 1615–1485 (C=C and C=N); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 11.84 and 9.28 (s, 2H, 2NH), 8.03–7.04 (m, 18H, ArH), 2.42 (s, 6H, $2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 161.34 and 159.75 (C=O), 149.63 (C–3), 142.60 (C–5), 118.05 (C–4), 18.62 and 17.92 (CH_3), 138.78, 136.52, 135.12, 130.89, 130.71, 130.59, 130.39, 129.60, 129.15, 129.10, 129.02, 128.67, 128.17, 126.93, 126.18, 125.69, 125.64, 124.85, 124.50, 122.93; Anal. Calcd. for $C_{31}H_{26}N_4O_2$: C, 76.52; H, 5.39; N, 11.51. Found: C, 76.61; H, 5.32; N, 11.53.

1,5-Diphenyl-N³,N⁴-bis(4-nitrophenyl)-1H-pyrazole-3,4-dicarboxamide (9l). (257 mg, 47%); mp 295–297°C; (was crystallized from EtOH/H_2O); IR (ν, cm^{-1}): 3468 and 3342 (NH), 3055 and 3006 (CH, aromatic), 1671 (C=O), 1627–1496 (C=C and C=N); ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 12.31 and 10.71 (s, 2H, 2NH), 8.18–6.52 (m, 18H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 162.80 and 160.14 (C=O), 148.52 (C–3), 144.80 and 144.10 (C=$\underline{C}$-NO_2), 143.25 (C–5), 119.47 (C–4), 142.50, 138.60, 130.11, 129.73, 129.04, 128.12, 126.85, 126.51, 126.45, 125.48, 125.40, 125.16, 122.51, 120.82; Anal. Calcd. for $C_{29}H_{20}N_6O_6$: C, 63.50; H, 3.68; N, 15.32. Found: C, 63.39; H, 3.72; N, 15.33.

1,5-Diphenyl-N³,N⁴-bis(4-fluorophenyl)-1H-pyrazole-3,4-dicarboxamide (9m). (400 mg, 81%); mp 227–228°C; (was crystallized from BuOH); IR (ν, cm^{-1}): 3356 (NH), 3039 and 3000 (CH, aromatic), 1679 (C=O), 1620–1499 (C=C and C=N); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 12.50 and 9.33 (s, 2H, 2NH), 7.75–6.98 (m, 18H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 161.62 and 159.15 (C=O), 161.12 and 158.68 (C=$\underline{C}$-F), 149.72 (C–3), 141.86 (C–5), 115.19 (C–4), 138.49, 130.53, 129.28, 129.01, 128.86, 128.15, 125.72, 122.57, 122.49, 121.88, 121.81, 116.05, 115.82, 115.41; Anal. Calcd. for $C_{29}H_{20}F_2N_4O_2$: C, 70.44; H, 4.08; N, 11.33. Found: C, 70.32; H, 4.12; N, 11.35.

1,5-Diphenyl-1H-pyrazole-3,4-dicarbonitrile (10). Compound **9a** of 0.306 g (1 mmol) was dissolved in 5 mL DMF, and 0.292 mL (4 mmol) $SOCl_2$ was added. After stirring for 2 h in ice bath and 12 h in room temperature, some ice water was added to the mixture. Precipitated solid product was filtered and purified from ethanol–water mixture by crystallization.

(259 mg, 96%); mp 148–149°C; IR (ν, cm^{-1}): 3020 (CH, aromatic), 2231 (CN), 1595–1466 (C=C and C=N); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.52–7.24 (m, 10H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 110.80 and 110.77 (CN), 149.05 (C–5), 98.20 (C–4), 137.61, 131.23, 130.03, 129.63, 129.41, 129.16, 128.39, 125.27, 124.92; Anal. Calcd. for $C_{17}H_{10}N_4$: C, 75.54; H, 3.73; N, 20.73. Found: C, 75.65; H, 3.69; N, 20.78.

2,3-Diphenyl-2H-pyrazolo[3,4-d]pyridazine-4,7-diamine (11). Compound **10** of 1 mmol was dissolved in 10 mL absolute ethanol. 0.5 mL anhydrous hydrazine was added and refluxed for 5 h. The solvent was evaporated and residue compound was washed with ether and water. The crude product was purified from ethanol–water by crystallization.

(208 mg, 69%); mp 292–294°C; IR (ν, cm^{-1}): 3453 and 3350 (NH), 3057 and 3024 (CH, aromatic), 1626–1492 (C=C and C=N); ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.46–7.18 (m, 10H, ArH), 4.81 (br. s, 4H, NH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 149.70 and 148.15 (N=$\underline{C}$-NH_2), 142.73 (C–3), 138.55, 130.22, 129.30, 129.22, 128.97, 128.78, 128.22, 126.57, 125.27, 114.22; Anal. Calcd. for $C_{17}H_{14}N_6$: C, 67.54; H, 4.67; N, 27.80. Found: C, 67.43; H, 4.75; N, 27.91.

Ethyl-1,5-diphenyl-1*H*-pyrazole-4-carboxylate (12). Compound **2** of 0.336 g (1 mmol) was heated at 200°C until gas exiting finished. Solid at the bottom

was washed with ether and water, respectively. The crude product was purified from ethanol–water mixture by crystallization. (131 mg, 45%); mp 125–126°C; IR (ν, cm^{-1}): 3064, (CH, aromatic), 2978 (CH, aliphatic), 1741 (C=O, ester), 1620–1482 (C=C and C=N); ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.19 (s, 1H, CH=N), 7.39–7.21 (m, 10H, ArH), 4.12 (q, J = 7.1 Hz, 2H, CH_2), 1.12 (t, J = 7.1 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 162.50 (C=O, ester), 144.61 (C–3), 144.01 (C–5), 120.16 (C–4), 139.15, 130.71, 130.55, 130.12, 129.78, 128.80, 126.45, 123.65; MS(CI) m/z 293.1 (M+1); Anal. Calcd. for $C_{18}H_{16}N_2O_2$: C, 73.95; H, 5.52; N, 9.58. Found: C, 73.82; H, 5.55; N, 9.57.

1,5-Diphenyl-1*H*-pyrazole-4-carboxylic acid (13). Compound **13** can be synthesized in two different methods.

Method. Compound **3** of 0.308 g (1 mmol) was heated at 250°C until carbon dioxide gas exiting finished. The residue solid was washed with water and purified from xylene by crystallization.

Method. Compound **12** of 0.292 g (1 mmol), 10 mL water, and 0.1 g (2.5 mmol) NaOH mixture was refluxed for about 1.5 h. Equal volume of water was added to mixture and cooled down to room temperature. The mixture was neutralized with 10% HCl solution and stirred approximately for half an hour to complete precipitation. Precipitated white product was filtered, washed with water, and purified from ethanol–water mixture by crystallization. (55–72%); mp 178–179 °C; IR (ν, cm^{-1}): 3420–2584 (OH, COOH), 3055 (CH, aromatic), 1689 (C=O), 1597–1498 (C=C and C=N); ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.12 (s, 1H, CH=N), 7.28–7.03 (m, 10H, ArH), ^{13}C NMR (100 MHz, DMSO-d_6) δ: 164.27 (C=O), 145.15 (C–3), 142.68 (C–5), 114.42 (C–4), 139.37, 130.74, 129.09, 129.04, 128.97, 128.90, 128.03, 125.52; MS(CI) m/z 265.1 (M+1); Anal. Calcd. for $C_{16}H_{12}N_2O_2$: C, 72.72; H, 4.58; N, 10.60. Found: C, 72.79; H, 4.51; N, 10.56.

2,3-Diphenyl-5,6-dihydro-2*H*-pyrazolo[3,4-d] pyridazine-4,7-dione (14). Compound **2** or **5a** of 1 mmol was dissolved in 10 mL dry toluene, and anhydrous hydrazine was added at 1/1 mole rate. The mixture was refluxed for about 5 h. Precipitate yellow product was filtered and purified from ethanol–water mixture by crystallization.

(60% and 73%); mp 316–318°C; IR (ν, cm^{-1}): 3158–2629 (NH), 3022 (CH, aromatic), 1642 (C=O), 1582–1490 (C=C and C=N); ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 10.40 (br. s, 1H, NH), 5.30 (br. s, 1H, NH), 7.70–7.01 (m, 10H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 161.79, 161.58, 156.58 and 152.33 (C=O↔ =C–OH), 145.34, 143.32, 143.04, 142.53, 139.48, 139.03, 131.22, 130.71, 129.60, 129.41, 129.37, 129.31, 128.92, 128.41, 128.34, 127.88, 126.70, 126.12, 120.70, 116.51; 114.02; Anal. Calcd. for $C_{17}H_{12}N_4O_2$: C, 67.10; H, 3.97; N, 18.41. Found: C, 66.93; H, 3.94; N, 18.48.

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