Chemistry of Heterocyclic Compounds, Vol. 40, No. 8, 2004

STUDIES ON REACTIONS OF CYCLIC OXALYL COMPOUNDS WITH HYDRAZINES OR HYDRAZONES. 2*. SYNTHESIS AND REACTIONS OF 4-BENZOYL-1-(4-NITROPHENYL)-5-PHENYL-1H-PYRAZOLE-3-CARBOXYLIC ACID

A. Sener[1], R. Kasimogullari[2], M. K. Sener[1], and H. Genc[1]

4-Benzoyl-1-(4-nitrophenyl)-5-phenyl-1H-pyrazole-3-carboxylic acid, obtained from the corresponding furan-2,3-dione and N-benzylidene-N'-(4-nitrophenyl)hydrazine, was converted via reactions of its acid chloride with various alcohols or N-nucleophiles into the corresponding ester or amide derivatives. The nitrile of the starting acid and 1-(4-aminophenyl)-4-benzoyl-5-phenyl-1H-pyrazole-3-carboxylic acid were also obtained. While cyclocondensation reactions of the two acids and the nitrile mentioned with hydrazines lead to pyrazolo[3,4-d]pyridazine derivatives, the reaction of starting acid with 2-hydrazinopyridine provided the hydrazonopyrazole acid derivative.

Keywords: cyclic oxalyl compounds, pyrazole, pyrazolopyridazine, quinoline.

In the last thirty years considerable interest has been focused on pyrazole chemistry, due to the versatile biological activities of pyrazole derivatives [2-4]. Our studies related to preparing pyrazole and fused pyrazole derivatives by the functionalization and cyclization reactions of some pyrazolecarboxylic acids, obtained from furandione **1**, with various nucleophiles was previously reported [1, 5, 6]. In the present study, we have attempted both to prove the reproducibility of the reaction of furandione **1** with another hydrazone and to extend our investigations related to preparing new pyrazole derivatives.

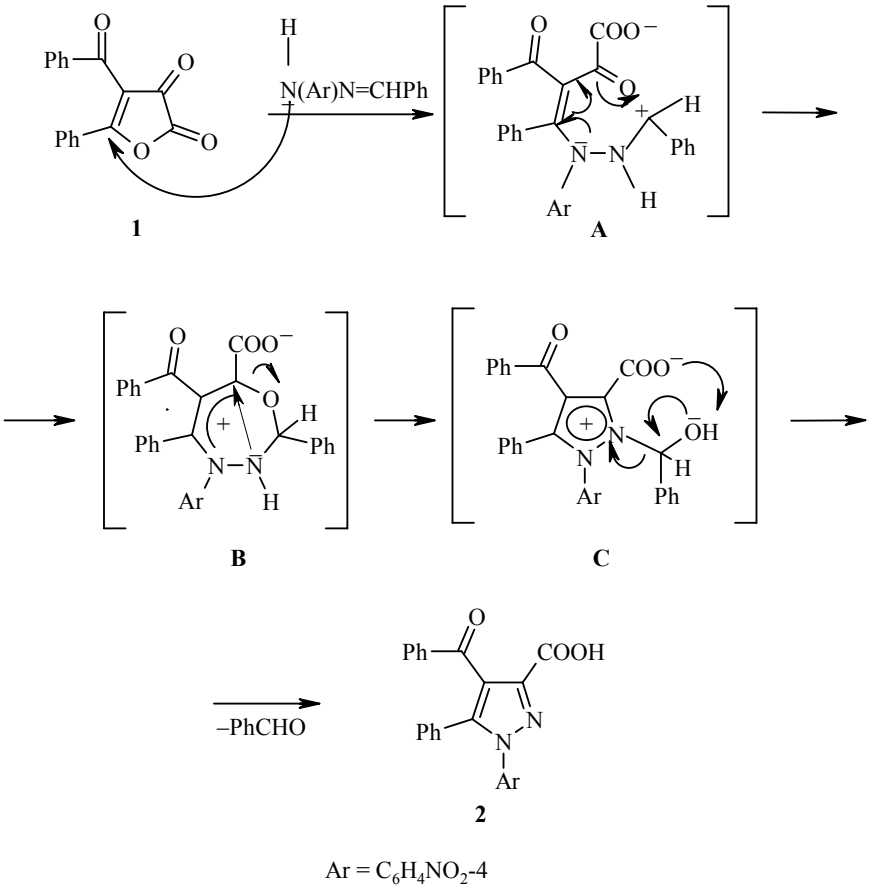
RESULTS AND DISCUSSION

Heating of furandione **1** and benzaldehyde 4-nitrophenylhydrazone (1/1 mol) for 75 min without any solvent led to the formation of the compound **2**, in *ca.* 45% yield. A reasonable pathway different from that discussed with phenylhydrazone [6] for reaction from furandione **1** to pyrazole carboxylic acid **2** is outlined briefly in Scheme 1.

* For Part 1 see [1].

[1] Yüzüncü Yil Üniversity, Art and Science Faculty, Chemistry Department, 65080 Van, Turkey; e-mail: asener_2002@jahoo.com. [2] Atatürk Üniversity, Art and Science Faculty, Chemistry Department, Erzurum, Turkey; e-mail: rahmikasimoglu@hotmail.com Published in Khimiya Geterotsiklicheskikh Soedinenii, No. 8, pp. 1201-1208, August, 2004. Original article submitted August 26, 2002.

Scheme 1



Ar = $C_6H_4NO_2$-4

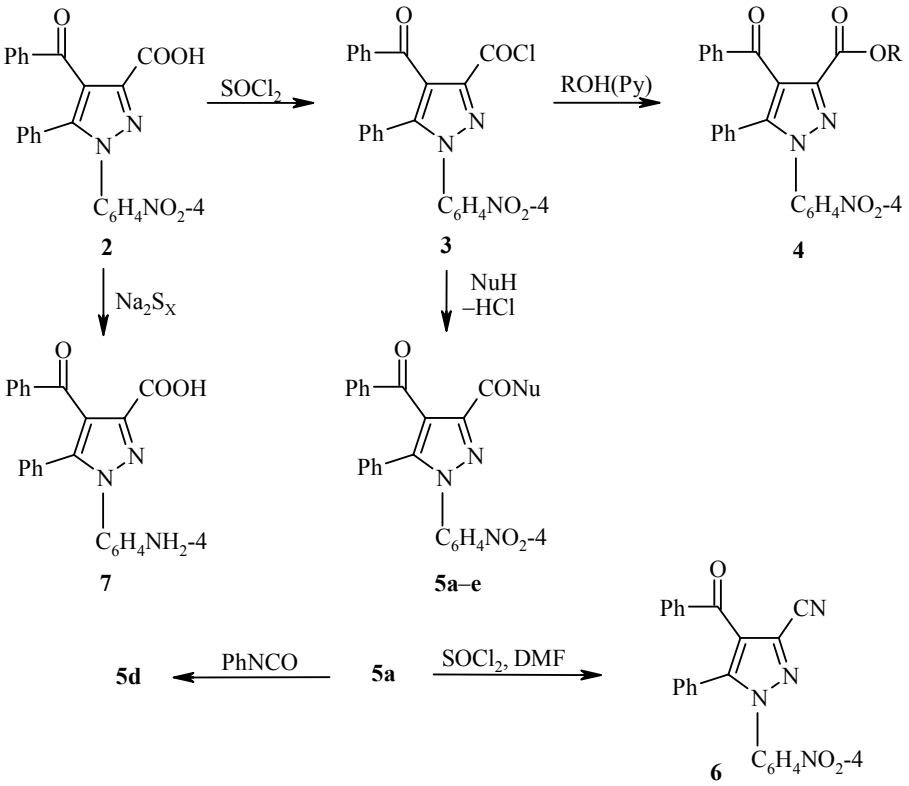
Ring opening for the formation of the first intermediate **A** should be initiated by a nucleophilic attack of the NH group adjacent to the phenyl ring of hydrazone at C(5) of the furandione ring similar to the reactions of furandione **1** with various H-active nucleophiles [7, 8]. Ring closure of the intermediate **A** to oxadiazepine intermediate **B** *via* addition of the N=CH–Ph group to the C=O moiety takes place by the catalytic effect of the carboxylic acid proton similar to the addition of azines to furandiones [9]. Rearrangement of the intermediate **B** generates the pyrazole carboxylate intermediate **C**, and finally loss of the benzaldehyde molecule gives compound **2**.

The acid **2** could be easily converted into the corresponding acid chloride **3**, ester **4**, amide **5**, and nitrile **6** by conventional chemical procedures. Reduction of **2** with sodium polysulfide led to the derivative of aminophenyl-substituted acid **7** (Scheme 2). The structures of the compounds thus obtained were confirmed by analytical and spectral data (see Experimental).

The correct structures of the unsymmetrically substituted urea derivatives **5d**,**e** were established by another chemical procedure consisting of the reaction of the primary amide **5a** with phenyl isocyanate, which resulted in the formation of the phenylurea derivative **5d**, originally prepared from the acid chloride **3** in the usual way.

Reactions of pyrazole dicarbonyl derivatives with hydrazines are convenient methods to build the pyrazolo[3,4-*d*]pyridazine systems [5, 10, 11]. Thus, the pyrazole acids **2**, **7** were cyclized with hydrazines to the pyrazolo[3,4-*d*]-pyridazinones **8a-d**, in 40-75% yields. Additionally, **8c** was also obtained by the second method consisting of reduction of **8a** with sodium polysulfide. In a similar way, pyrazole-3-carbonitrile **6** with

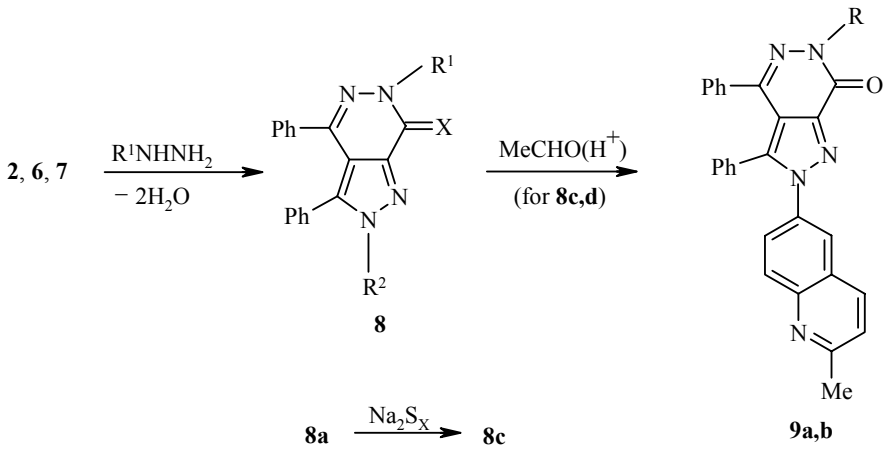
Scheme 2



4 R = *i*-Pr; **5 a** Nu = NH_2, **b** Nu = NHEt, **c** Nu = NEt_2, **d** Nu = NHCONHPh, **e** Nu = NHCONHBu-*t*

anhydrous hydrazine in boiling methanol containing a catalytic amount of sodium methoxide was also cyclized to the 7-aminopyrazolo[3,4-*d*]pyridazine derivative **8e**. Cyclization reactions of compounds **8c**,**d** with acetaldehyde in strong acidic medium lead to quinoline derivatives **9a**,**b** (Scheme 3). Structure elucidation of compounds **8a-e** and **9a**,**b** is based mainly on ^{13}C NMR spectroscopy (see Experimental).

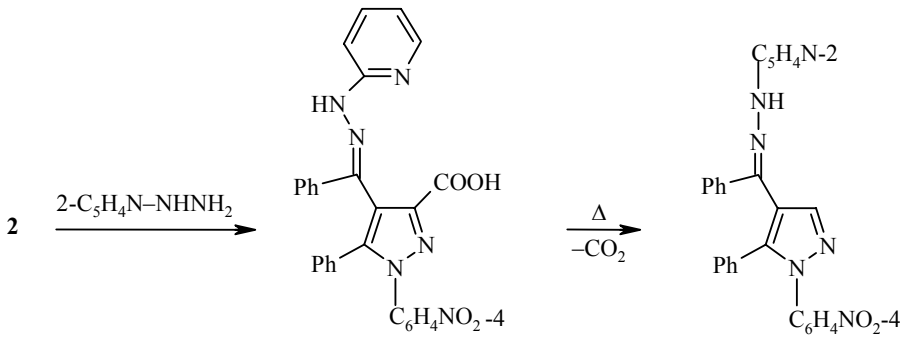
Scheme 3



8a,**c** R^1 = Ph, **b**, **d**, **e** R^1 = H; **a**, **b**, **e** R^2 = $C_6H_4NO_2$-4, **c**, **d** R^2 = $C_6H_4NH_2$-4;
a-d X = O, **e** X = NH; **9 a** R = H, **b** R = Ph

On the other hand, the reaction of **2** with 2-hydrazinopyridine instead of phenylhydrazine or hydrazine hydrate did not give the corresponding pyrazolopyridazine derivative. Surprisingly, however, 2-hydrazinopyridine was added to **2** to yield a new pyrazole acid **10** containing a hydrazone group. The failure or the difficulty in forming the pyridazine nucleus from **2** with 2-hydrazinopyridine can be explained by the low nucleophilicity of the nitrogen atom adjacent to the pyridine ring. Additionally, decarboxylation of **10** on an oil bath at elevated temperatures led to cleavage of the C–C bond with loss of CO_2, finally yielding the corresponding hydrazonopyrazole derivative **11** (Scheme 4).

Scheme 4



Compounds **10** and **11** show characteristic IR absorption bands at 3450 (NH), 1681 (C=N) and 3438 (NH), 1679 cm^{-1} (C=N), respectively. The IR spectra of compound **10** showed no absorption bands corresponding to the COOH group such as 3300-2500 (b, OH, COOH) and 1700-1750 cm^{-1} (C=O, COOH) like that of 4-benzoyl-1,5-diphenylpyrazole-3-carboxylic acid [6]. However, absorption bands at approximately 1620 and 1579 cm^{-1} corresponding to an ionized carboxylate group [12] were observed. From its IR spectrum, it may be deduced that compound **10** exists as the betaine in the solid state, but the ^{13}C NMR signal for the carboxyl group of **10** appears at nearly equivalent chemical shift values to that observed with carboxylic acid groups of **2** and **7**. Obviously in solution the classical acid form is predominant (see Experimental).

EXPERIMENTAL

Solvents were dried by refluxing with the appropriate drying agents and distilled before use. Melting points were determined on an Electrothermal Gallenkamp apparatus and are uncorrected. Microanalyses were performed on a Carlo Erba Elemental Analyser Model 1108. The IR spectra were obtained in potassium bromide pellets using a Mattson 1000 FTIR spectrometer. The ^{1}H and ^{13}C NMR spectra were recorded on Varian (200 MHz) and Varian (50 MHz) spectrometers, respectively, using TMS as an internal standard. All experiments were followed by TLC using DC Alufolien Kieselgel 60 F 254 Merck and Camag TLC lamp (254/366 nm).

4-Benzoyl-1-(4-nitrophenyl)-5-phenyl-1H-pyrazole-3-carboxylic Acid (2). An equimolar mixture of furandione **1** (0.278 g, 1 mmol) and (4-nitrophenylhydrazono) (phenyl) methane (0.241 g, 1 mmol) was heated without a solvent at 100-110°C for 75 min (up to disappearance of benzaldehyde odor). After cooling to room temperature, the residue was treated with dry toluene and the formed crude product was recrystallized from ethanol to give 0.186 g (45%) of a colorless solid; mp 210°C (decomp.). IR spectrum, ν, cm^{-1}: 3400-2500 (b, OH, COOH), 1717 (C=O, COOH), 1680 (C=O, benzoyl). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 8.3-7.2 (m, ArH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 192.26 (C=O, benzoyl); 163.83 (C=O, COOH); 148.50 (C–NO_2);

145.33 (C(3)); 145.22 (C(5)); 145.09 (C(1) of $C_6H_4NO_2$); 139.31 (C–Ph); 135.32, 131.46, 130.90, 130.50, 130.44, 129.13 (C–Ph); 128.22, 126.34, 125.41 (C(4)). Found, %: C 66.69; H 3.69; N 10.20. $C_{23}H_{15}N_3O_5$. Calculated, %: C 66.83; H 3.66; N 10.16.

4-Benzoyl-1-(4-nitrophenyl)-5-phenyl-1H-pyrazole-3-carbonyl Chloride (3). Acid **2** (0.413 g, 1 mmol) and thionyl chloride (1 ml, 13.8 mmol) were refluxed on a steam bath for 5 h. After cooling, the crude precipitate was filtered off and recrystallized from a mixture of cyclohexane and carbon tetrachloride, yield 0.281 g (65%); mp 190°C. IR spectrum, ν, cm^{-1}: 1757 (C=O, acyl), 1676 (C=O, benzoyl). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 190.74 (C=O, benzoyl); 162.88 (C=O, acyl); 148.69 (C–NO_2); 146.47 (C(3)); 146.40 (C(5)); 144.48 (C(1) of $C_6H_4NO_2$); 138.30 (C–Ph); 135.26, 131.72, 130.98, 130.67, 130.49, 130.00, 127.90 (C–Ph); 127.11, 125.98, 125.72 (C(4)). Found, %: C 64.09; H 3.26; Cl 8.17; N 9.69. $C_{23}H_{14}N_3O_4Cl$. Calculated, %: C 63.97; H 3.27; Cl 8.21; N 9.73.

Isopropyl 4-Benzoyl-1-(4-nitrophenyl)-5-phenyl-1H-pyrazole-3-carboxylate (4). The acid chloride **3** (0.431 g, 1 mmol) and a moderate excess of isopropyl alcohol were refluxed together with a catalytic amount of pyridine for 2.5 h. After cooling, the solution was acidified by adding diluted hydrochloric acid (12%) to give a crude solid, which was recrystallized from the same alcohol. The yield 0.342 g (75%); mp 156°C. IR spectrum, ν, cm^{-1}: 1741 (C=O, ester), 1676 (C=O, benzoyl). Found, %: C 68.75; H 4.67; N 9.20. $C_{26}H_{21}N_3O_5$. Calculated, %: C 68.56; H 4.65; N 9.23.

4-Benzoyl-1-(4-nitrophenyl)-5-phenyl-1H-pyrazole-3-carboxamide (5a). A moderate stream of gaseous ammonia was allowed to bubble through a solution of acid chloride **3** (0.432 g, 1 mmol) in 20 ml of carbon tetrachloride during 0.5 h with ice-cooling. Then the crude precipitate was filtered off and recrystallized from methanol to give 0.289 g (70%) of **5a**; mp 210°C. IR spectrum, ν, cm^{-1}: 3438 (NH_2), 1674 (C=O, benzoyl), 1625 (C=O, amide). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 192.45 (C=O); 163.34 (C=O, amide); 148.17 (C–NO_2); 147.28 (C(3)); 145.49 (C(5)); 144.97 (C(1) of $C_6H_4NO_2$); 139.13 (C–Ph); 134.59, 131.24, 131.01, 130.74, 130.32, 129.64, 128.78 (C–Ph); 126.68, 125.82, 124.64 (C(4)). Found, %: C 67.19; H 3.90; N 13.64. $C_{23}H_{16}N_4O_4$. Calculated, %: C 66.99; H 3.91; N 13.59.

Amides 5b,c and Ureas 5d,e. (General Procedure). An equimolar mixture of the acid chloride **3** (0.431 g, 1 mmol) and the corresponding amine or urea (1 mmol) was refluxed in xylene for 3-6 h. After evaporation, the oily residue was treated with dry ether and the formed crude product was recrystallized.

N-Ethyl-4-benzoyl-1-(4-nitrophenyl)-5-phenyl-1H-pyrazole-3-carboxamide (5b). Reflux time 3 h (ethylamine). Yield 0.34 g (77%); mp 177°C (aqueous EtOH). IR spectrum, ν, cm^{-1} 3259 (NH), 1676 (C=O), 1631 (C=O, amide). Found, %: C 67.99; H 4.61; N 12.68. $C_{25}H_{20}N_4O_4$. Calculated, %: C 68.17; H 4.58; N 12.72.

4-Benzoyl-N,N-diethyl-1-(4-nitrophenyl)-5-phenyl-1H-pyrazole-3-carboxamide (5c). Reflux time 3.5 h (diethylamine). Yield 0.281 g (60%); mp 176°C (EtOH). IR spectrum, ν, cm^{-1}: 1670 (C=O), 1632 (C=O). Found, %: C 69.05; H 5.19; N 11.89. $C_{27}H_{24}N_4O_4$. Calculated, %: C 69.22; H 5.16; N 11.96.7

N-[4-Benzoyl-1-(4-nitrophenyl)-5-phenyl-1H-pyrazole-3-carbonyl]-N'-phenylurea (5d). A. Reflux time 4 h (phenylurea). Yield 0.186 g (35%); mp 223°C (EtOH). IR spectrum, ν, cm^{-1}: 3405, 3320 (NH), 1745 (C=O, urea), 1669 (C=O), 1628 (C=O). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 192.27 (C=O); 163.65 (C=O); 151.05 (C=O, urea); 149.98 (C–NO_2); 146.17 (C(3)); 145.42 (C(1) of $C_6H_4NO_2$); 145.28 (C(5)); 140.05 (N–Ph); 138.77 (C–Ph); 135.05, 132.75, 132.05, 131.88, 131.57, 131.09, 130.75, 130.43, 127.98 (C–Ph); 126.05, 125.17, 122.76, 122.35 (C(4)). Found, %: C 67.65; H 4.03; N 13.22. $C_{30}H_{21}N_5O_5$. Calculated, %: C 67.79; H 3.98; N 13.18.

B. The acid amide **5a** (0.412 g, 1 mmol) and phenylisocyanate (0.2 ml, 1.8 mmol) were refluxed in xylene for 6 h. Then the solvent was evaporated and the residue was recrystallized from ethanol to give 0.425 g (80%) of **5d**, identical in mp and IR spectrum with the product obtained as described above.

N-[4-Benzoyl-1-(4-nitrophenyl)-5-phenyl-1H-pyrazole-3-carbonyl]-N'-(*tert*-butyl)urea (5e). Reflux time 4 h (*tert*-butylurea). Yield 0.286 g (56%); mp 244°C (*n*-PrOH). IR spectrum, ν, cm^{-1}: 3380-3340 (NH), 1727 (C=O, urea), 1668 (C=O), 1627 (C=O). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 8.9 (s, 1H, NH); 8.6 (s,

1H, NH); 8.2-7.3 (m, 14H, ArH); 1.3 (s, 9H, CH_3). Found, %: C 65.93; H 4.95; N 13.65. $C_{28}H_{25}N_5O_5$. Calculated, %: C 65.74; H 4.93; N 13.69.

4-Benzoyl-1-(4-nitrophenyl)-5-phenyl-1H-pyrazole-3-carbonitrile (6). A cold solution of the acid amide **5a** (0.412 g, 1 mmol) in a mixture of DMF (0.7 ml) and $SOCl_2$ (0.15 ml) was stirred at 0-5°C for 2 h. After heating to room temperature, stirring was continued overnight, then the reaction mixture was poured onto crushed ice and the separated solid filtered off, washed with water, and recrystallized from *n*-PrOH to give 0.217 g (55%) of **6** mp 214°C. IR spectrum, ν, cm^{-1}: 2265 (CN), 1670 (C=O). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 189.01 (C=O); 148.75 (C–NO_2); 146.82 (C(1) of $C_6H_4NO_2$); 144.21 (C(5)); 137.80 (C(3)); 134.95, 131.77, 131.43, 130.89, 130.34, 129.72, 129.17 (C–Ph); 127.77 (C(4)); 127.15, 126.90 (C–Ph); 113.17 (CN). Found, %: C 70.19; H 3.61; N 14.18. $C_{23}H_{14}N_4O_3$. Calculated, %: C 70.05; H 3.58; N 14.21.

1-(4-Aminophenyl)-4-benzoyl-5-phenyl-1H-pyrazole-3-carboxylic Acid (7). A cold solution of sodium polysulfide (10 mmol), prepared from $Na_2S{\cdot}9H_2O$ (2.5 g, 10 mmol) with powdered sulfur (0.7 g) in boiling water, was added to a solution of **2** (4.13 g, 10 mmol) in ethanol with stirring. The reaction mixture was refluxed on a steam bath for 60 min. After cooling and acidification with concentrated HCl, it was refluxed again for 30 min to precipitate sulfur, cooled, and the separated solid filtered off. Then, the filtrate was made alkaline by adding concentrated aqueous ammonia (slight excess) and kept in the refrigerator overnight. The crude precipitate was washed with water and recrystallized from a mixture of ethanol and water to give 1.96 g (51%) of **7** mp 228°C. IR spectrum, ν, cm^{-1}: 3438 (NH_2), 3300-2500 (b, OH, COOH), 1727 (C=O, COOH), 1672 (C=O, benzoyl). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 192.87 (C=O); 164.22 (COOH); 150.95 (NH_2–Ph); 144.52 (C(3)); 143.42 (C(5)); 139.56 (C(1) in $C_6H_4NH_2$-4); 135.10, 131.37, 130.80, 130.71 (C–Ph); 130.41, 130.10, 129.94, 128.92 (C–Ph); 128.58, 123.99, 115.08 (C(4)). Found, %: C 72.25; H 4.45; N 10.93. $C_{23}H_{17}N_3O_3$. Calculated, %: C 72.05; H 4.47; N 10.96.

2,6-Dihydropyrazolo[3,4-*d*]pyridazin-7-ones 8a-d. (General Procedure). An equimolar mixture of **2** and the respective hydrazine was refluxed in xylene for 1-4 h. After the solvent was removed by evaporation, the oily residue was treated with ether and the formed crude product was recrystallized.

2-(4-Nitrophenyl)-3,4,6-triphenyl-2,6-dihydropyrazolo[3,4-*d*]pyridazin-7-one (**8a**). Reflux time 3 h (phenylhydrazine). Yield 0.364 g (75%); mp 267°C (methanol). IR spectrum, ν, cm^{-1}: 1686 (C=O). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 156.60 (C=O); 148.68 (C–NO_2); 145.48 (C(7a)); 145.17 (C(4)); 145.035 (C(3)); 142.96 (C(1) in $C_6H_4NO_2$); 141.87 (C(1) in N–Ph); 135.14, 131.66, 131.07 (C–Ph); 130.03, 129.97, 129.89, 129.03, 128.92, 128.71 (C–Ph); 127.87, 127.26, 125.67, 118.59 (C(3a)). Found, %: C 71.55; H 3.97; N 14.38. $C_{29}H_{19}N_5O_3$. Calculated, %: C 71.74; H 3.94; N 14.42.

2-(4-Nitrophenyl)-3,4-diphenyl-2,6-dihydropyrazolo[3,4-*d*]pyridazin-7-one (8b). Reflux time 1 h (hydrazine hydrate). Yield 0.299 g (73%); mp 305°C (*n*-BuOH). IR spectrum, ν, cm^{-1}: 3300-2800 (b, NH⇄OH), 1677 (C=O). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 157.74 (C=O); 148.90 (C–NO_2); 145.37 (C(7a)); 144.43 (C(4)); 142.51 (C(3)); 141.19 (C(1) in $C_6H_4NO_2$), 135.88, 132.38, 131.09, 130.06, 129.99 (C–Ph); 129.81, 129.23, 129.14, 129.05 (C–Ph); 126.17, 118.76 (C(3a)). Found, %: C 67.31; H 3.71; N, 17.17. $C_{23}H_{15}N_5O_3$. Calcula-ted, %: C 67.48; H 3.69; N 17.11.

2-(4-Aminophenyl)-3,4,6-triphenyl-2,6-dihydropyrazolo[3,4-*d*]pyridazin-7-one (8c). A. Reflux time 4 h (phenylhydrazine). Yield 0.205 g (45%); mp 290°C (*n*-BuOH). IR spectrum, ν, cm^{-1}: 3489-3387 (NH_2), 1667 (C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 7.6-6.6 (m, 19H, ArH); 3.9-2.6 (b, 2H, NH_2). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 157.77 (C=O); 148.99 (C–NH_2); 146.23 (C(7a)); 144.87 (C(4)); 143.93 (C(3)); 141.69 (C(1) in N–Ph); 136.25 (C(1) in $C_6H_4NH_2$); 132.53, 131.92 (C–Ph); 130.80, 130.66, 130.46, 130.23 (C–Ph); 130.04, 129.61, 129.42, 129.10, 128.11, 118.40 (C(3a)); 116.72. Found, %: C 76.75; H 4.66; N 15.41. $C_{29}H_{21}N_5O$. Calculated, %: C 76.47; H 4.65; N 15.37.

B. Pyridazinone **8a** (0.485 g, 1 mmol) and Na_2S_X (1 mmol) were refluxed in a mixture of EtOH and water on a steam bath for about 1 h. The crude product which precipitated in boiling solvents was filtered off and recrystallized from *n*-BuOH to give 0.273 g (60%) of **8c**, identical in mp and IR spectrum with the product obtained as described above.

2-(4-Aminophenyl)-3,4-diphenyl-2,6-dihydropyrazolo[3,4-*d*]pyridazin-7-one (8d). Reflux time 3 h (hydrazine hydrate). Yield 0.152 g (40 %); mp 342°C (EtOH). IR spectrum, ν, cm^{-1}: 3489-3308 (NH_2), 3250-2800 (b, NH⇄OH), 1659 (C=O). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 157.98 (C=O); 151.17 (C–NH_2); 145.37 (C(7a)); 143.18 (C(4)); 141.54 (C(3)); 136.19 (C(1) in $C_6H_4NH_2$); 132.35, 130.37 (C–Ph); 130.06, 129.83, 129.75, 129.42, 129.08, 128.97 (C–Ph); 128.79, 118.01 (C(3a)); 114.86. Found, %: C 72.99; H 4.54; N 18.41. $C_{23}H_{17}N_5O$. Calculated, %: C 72.81; H 4.52; N 18.46.

[2-(4-Nitrophenyl)-3,4-diphenyl-2H-pyrazolo[3,4-*d*]pyridazin-7-yl]amine (8e). Nitrile **6** (0.394 g, 1 mmol) and anhydrous hydrazine (0.032 g, 1 mmol) were refluxed in methanol containing a catalytic amount of sodium methoxide on an oil bath for 15 h. After cooling to room temperature, the crude precipitate was isolated by filtration and recrystallized from *n*-BuOH. Yield 0.225 g (55%); mp 315°C. IR spectrum, ν, cm^{-1}: 3300-3000 (NH), 1663 (C=NH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 158.05 (C=NH); 149.11 (C–NO_2); 146.77 (C(1) in $C_6H_4NO_2$); 146.40 (C(7a)); 144.31 (C(3)); 140.88 (C(4)); 133.07, 132.03 (C–Ph); 131.99, 131.04 (C–Ph); 130.71, 130.23, 129.59, 129.17, 128.75, 127.25, 123.28 (C(3a)). Found, %: C 67.58; H 4.02; N 20.51. $C_{23}H_{16}N_6O_2$. Calculated, %: C 67.64; H 3.95; N 20.58.

2-(2-Methylquinolin-6-yl)-3,4-diphenyl-2,6-dihydropyrazolo[3,4-*d*]pyridazin-7-one (9a). To a cold solution of compound **8d** (1 mmol) in concentrated HCl (15-20 ml), acetaldehyde (0.1 ml, 2 mmol) and nitrobenzene (0.123 g, 1 mmol) were added with stirring, and stirring was continued at room temperature for 2 h. Then, the reaction mixture was refluxed on a steam bath for 10 h with stirring and filtered. The filtrate was made alkaline by adding concentrated aqueous ammonia and kept in a refrigerator overnight. The separated solid was filtered off, washed with water, and recrystallized from a mixture of methanol and water. Yield 0.193 g (45%); mp 280°C. IR spectrum, ν, cm^{-1}: 3450-2750 (NH⇄OH), 1663 (C=O). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 162.36 (C=O); 157.95 (C(2')); 148.26 (C(8'a)); 145.37 (C(7a)); 143.99 (C(4)); 142.29 (C(3)); 138.20, 137.54, 136.04, 132.33, 130.72, 130.48 (C–Ph); 130.08, 129.81 (C–Ph); 129.58, 129.42, 129.15, 128.91, 128.76, 127.34, 125.03, 118.40 (C(3a)); 26.69 (Me). Found, %: C 75.30; H 4.48; N 16.27. $C_{27}H_{19}N_5O$. Calculated, %: C 75.51; H 4.46; N 16.31.

2-(2-Methylquinolin-6-yl)-3,4,6-triphenyl-2,6-dihydropyrazolo[3,4-*d*]pyridazin-7-one (9b) was obtained similarly to **9a** from **8c**. Reflux time 8 h, yield 0.237 g (46%); mp 244°C (methanol). IR spectrum, ν, cm^{-1}: 1666 (C=O). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 162.48 (C=O); 156.59 (C(2')); 148.35 (C(8'a)); 145.60 (C(7a)); 144.18 (C(4)); 143.46 (C(3)); 142.80, 138.26, 137.47, 135.51, 132.41, 130.93, 130.83, 130.48 (C–Ph); 130.39, 130.23, 129.69, 129.32, 129.21, 128.91 (C–Ph); 128.11, 127.40, 127.27, 125.12, 118.14 (C(3a)); 26.71 (Me). Found, %: C 78.17; H 4.54; N 13.82. $C_{33}H_{23}N_5O$. Calculated, %: C 78.41; H 4.55; N 13.86.

1-(4-Nitrophenyl)-5-phenyl-4-[phenyl(pyridin-2-ylhydrazono)methyl]-1H-pyrazole-3-carboxylic Acid (10). Compound **2** (0.413 g, 1 mmol) and 0.109 g (1 mmol) of 2-hydrazinopyridine were refluxed in xylene on an oil bath for 3 h. The solvent was evaporated and the remaining oily residue was treated with ether to give a crude product which was recrystallized from ethanol. Yield 0.434 g (86%); mp 309°C (decomp.). IR spectrum, ν, cm^{-1}: 3450 (NH), 1681 (C=N–), 1620, 1579 (COO^-). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 10.1 (b, acidic proton); 8.9 (b, 1H, NH); 8.3-6.8 (m, 18H, ArH). ^{13}C NMR spectrum (DMSO-d_6),δ, ppm: 163.99 (COO^-); 156.82 (C(2'), Py); 149.25 (C–NO_2); 148.22 (C=N–); 145.88 (C(3)); 145.82 (C(6'), Py); 144.97 (C(5)); 139.84 (C(1) in $C_6H_4NO_2$); 139.76, 138.81, 131.16, 131.08 (C–Ph); 130.83, 130.43, 129.93, 129.61 (C–Ph); 128.08, 127.36, 126.20, 126.10, 117.37, 109.08 (C(4)). Found, %: C 66.51; H 4.05; N 16.73. $C_{28}H_{20}N_6O_4$. Calculated, %: C 66.66; H 4.00; N 16.66.

[1-(4-Nitrophenyl)-5-phenyl-1H-pyrazol-4-yl(phenyl)methanone-N-pyridin-2-ylhydrazone (11). Compound **10** (0.46 g, 1 mmol) was heated to 310-315°C on an oil bath for about 0.5 h without a solvent. After cooling to room temperature, the residue was treated with ether to give a crude product which was recrystallized from ethanol. Yield 0.253 g (55%); mp 320°C. IR spectrum, ν, cm^{-1}: 3438 (NH), 1679 (C=N–). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 156.65 (C(2'), Py); 155.22 (C=N–); 150.84 (C(6'), Py); 149.09 (C–NO_2); 145.51

(C(3)); 145.24 (C(5)); 144.47 (C(1) in $C_6H_4NO_2$); 143.24 (C–Ph); 140.46, 135.18, 132.37, 131.28, 130.39, 129.89, 129.32, 129.24, 128.70 (C–Ph); 126.77, 125.83, 124.08, 118.70 (C(4)). Found, %: C 70.53; H 4.39; N 18.20. $C_{27}H_{20}N_6O_2$. Calculated, %: C 70.42; H 4.38; N 18.25.

The authors thank the research fund of Y. Yil University for financial support.

REFERENCES

1. A. Sener, R. Kasımogullari, M. K. Sener, I. Bildirici, and Y. Akcamur, *J. Heterocycl. Chem*., **39**, 869 (2002).
2. A. M. Farghaly, N. S. Habib, M. A. Khalil, O. A. El-Sayed, and J. Alexandria, *Pharm. Sci.*, **3**, 90 (1989).
3. R. N. Mahajan, F. H. Havaldar, and P. S. Fernandes, *J. Indian Chem. Soc*., **68**, 245 (1991).
4. P. G. Baraldi, S. Manfredini, R. Romagnoli, L. Stevanato, A. N. Zaid, and R. Manservigi, *Nucleosides and Nucleotides*, **17**, 2165 (1998).
5. Y. Akcamur, A. Sener, A. M. Ipekoglu, and G. Kollenz, *J. Heterocycl. Chem*., **34**, 221 (1997).
6. Y. Akcamur, G. Penn, E. Ziegler, H. Sterk, G. Kollenz, K. Peters, E. M. Peters, and H. G. von Schnering, *Monatsh. Chem*., **117**, 231 (1986).
7. Y. Akcamur, B. Altural, E. Saripinar, G. Kollenz, O. Kappe, K. Peters, E. M. Peters, and H. G. Schnering, *J. Heterocycl. Chem*., **25**, 1419 (1988).
8. B. Altural, Y. Akcamur, E. Saripinar, I. Yildirim, and G. Kollenz, *Monatsh. Chem*., **120**, 1015 (1989).
9. E. E. Schweizer, J. E. Hayes, K. J. Lee, and A. L. Rheingold, *J. Org. Chem*., **52**, 1324 (1987).
10. J. P. Marquet, J. D. Bourzat, J. Andre-Loisfert, and E. Bisagni, *Tetrahedron*, **29**, 435 (1973).
11. A. S. Shawali, *J. Heterocycl. Chem*., **14**, 375 (1977).
12. G. C. Bassler, T. C. Morrill, and R. M. Silverstein (editors), *Spectrometric Identification of Organic Compounds*, J. Wiley and Sons, New York, NY (1991), p. 118.