

Synthesis of Some Pyrazolo-Pyridazine Compounds

Adem ÖNAL

Gaziosmanpaşa University, Arts and Sciences Faculty,

Department of Chemistry, Tokat-TURKEY

Yunus AKÇAMUR, Behzat ALTURAL

Erciyes University, Arts and Sciences Faculty,

Department of Chemistry, Kayseri-TURKEY

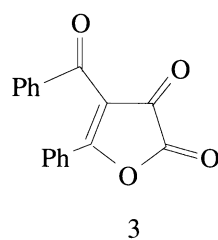
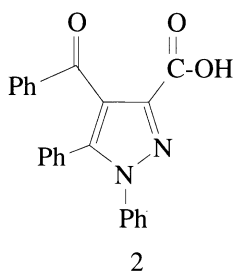
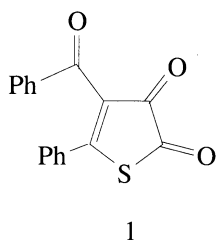
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Addition of **1** to two moles of phenylhydrazine gives 1,2,4,6- tetraphenyl-(2,3-d)-pyrazolo-5,6-pyridazine-7-one **4** isomer compound **1**, 2,3,5-tetraphenyl-(2,3-d) pyrazolo-5,6-pyridazine-7-one **5** of **4** was synthesized by the reaction of **2** with phenylhydrazine. 3,4- Diphenyl-(2,3-d)-pyrazolo-(1H,6H)-pyridazine-7-one **6** was also obtained in two different ways. Reaction of **1** and 4-benzoyl-5 phenyl- furan-2,3-dione **3** with hydrazinium hydrate furnished compound **6**. The structures of **4,5** and **6** were determined by the ^{13}C -NMR, IR spectra and elemental analysis. These new isomer and condensed compounds synthesized in this study are important for heterocyclic chemistry.

Introduction

4-Benzoyl-5-phenyl-thiophene-2,3-dione **1**, 4-benzoyl-1,5-phenyl- pyrazolo-3-carboxylic acid **2** and 4-benzoyl-5-phenyl-furan-2,3- dione **3** are important starting compounds in syntehetic organic chemistry.^{1,2,3,4}

In this study, compounds 3,4-diphenyl-(2,3-d)-pyrazolo (1H, 6H)-5,6- pyridazin-7-one **6** and 1,3,4,6-tetraphenyl-(2,3-d)-pyrazolo-5,6- pyridazine-7-one **4** were synthesized from the reaction of hydrazinium hydrate and phenylhydrazine with 4-benzoyl-5-phenyl-thiophene-2,3-dione **1**, respectively. The isomer compound **5** of **4** was obtained from the reaction of phenylhydrazine with 4-benzoyl-5-phenyl-furan-2,3- dione **3** and **1**. **4,5** and **6** were synthesized for the first time. The results obtained were interpreted.



Experimental Section

Melting points were determined by use of a Buchi melting point apparatus and not corrected. The compounds were routinely checked for their homogeneity by TLC using Kieselgel *GF*₂₅₄60 as adsorbend. The IR spectra were recorded on a Shimadzu spectrophotometer model 435 V-04 as pellets. The ¹H-NMR and ¹³C-NMR spectra were recorded with Varian H-100 FT and Varian H-200 instruments using TMS as internal reference. The elemental analysis were determined with Carlo-Erba 1106 of Hewlett Packard model 105. The solvents were evaporated with rotary evaporator Buchi RE model 111.

Solvents and other chemical reagents were from Merck and aldrich. Solvents were distilled before using.

1,3,4,6-Tetraphenyl- (2,3-d) Pyrazolo-5,6-pyridazine-7-one 4:

4-Benzoyl-5-phenyl-thiophene-2,3-dione [0,29 g (0,6 mmol)] **1** was dissolved in 25 ml of benzene and 0,15 ml (1.52 mmol) of phenylhydrazine was dropped in this solution at room temperature and refluxed for 1 h. After evaporation, the oily residue was stirred on a magnetic stirrer with ether. The precipitate was separated ether by filtering and recrystallized from distilled ethanol to give product **4** (25%) as a white crystal having m. p. 250-251 °C:

Anal.for *C*₂₉*H*₂₀*N*₄*O*

Calc.: C, 79.01; H, 4.65; N, 12.57

Found: C, 79.09; H, 4.54; N, 12.72

IR (KBr, cm⁻¹): 3100-3050 (aromatic C-H stretching), 1700-1690 (C=O stretching), 1620-1600 (C=N and aromatic C=C stretching).

¹³C-NMR (200 MHz, DMSO-d₆): 139.0 (N1-Ph), 158.5 (C3), 144. 1 (C4), 151.5 (N6-Ph), 158.5 (C7), 133.2 (C8), 119.5 (C9).

1,2,3,5- Tetrphenyl-(2,3-d)-pyrazolo-5,6-pyridazine-7-one 5:

4-Benzoyl-1,5-diphenyl-pyrazolo-3-carboxylic acid [1.1g (2,71 mmol)] **2** was dissolved in 25 ml of xylene and 0.3 ml (3 mmol) of phenylhydrazine was dropped in this solution at room temperature and refluxed for 2 h. After cooling, the precipitate was separated by filtering and recrystallized from ethanol to give product **5** (55%) as a white crystal, m.p. 218 °C:

Anal.for *C*₂₉*H*₂₀*N*₄*O*

Calc.: C, 79.91; H, 4.76; N, 12.69

Found: C, 79.09; H, 4.54; N, 12.72

IR (KBr, cm⁻¹): 3050 (aromatic C-H stretching), 1690-1595 (C=O and aromatic C=N stretching), 1360, (C-N Stretching).

3,4-Diphenyl-(2,3-d)-Pyrazolo-(1H,6H)-pyridazine-7-one 6:

4-Benzoyl-5-phenyl-thiophene-2,3-dione [0.5 g (1,7 mmol)] **1** was dissolved in 25 ml of benzene. More than equivalent value required of hydrazinium hydrate was added to this solution and stirred by magnetic stirrer at room temperature for 12 h. The precipitate was filtered and recrystallized from ethanol to give product **6** (24%) as white needle crystals, m.p. 307-308 °C.

Anal.for *C*₁₇*H*₁₂*N*₄*O*

Calc.: C, 79.94; H, 4.32; N, 19.42

Found: C, 70.83; H, 4.16; N, 19.44

IR (KBr, cm⁻¹): 3300-2700 (N-H stretching), 1700-1640 (C=O stretching), 1260-1200 (N-N stretching).

¹³C-NMR (200 MHz, DMSO-d₆): 143.1 (C3,4), 134.6(C3, 4-Ph), 153.5 (C7), 131.0 (C8), 129-127 (other carbon atoms of two phenyl groups)

The Synthesis of 6 from 3:

4-Benzoyl-5-phenyl-furan-2,3-dione [0,5 g (1.8 mmol)] **3** dissolved in 25 ml of xylene. More than equivalent value required of hydrazinium hydrate was added to this solution and refluxed for 1 h. After filtering, the precipitate was recrystallized from methanol to give product **6** (25%) as a white thin crystal, m. p. 307-308 °C

Anal. for $C_{17}H_{12}N_4O$

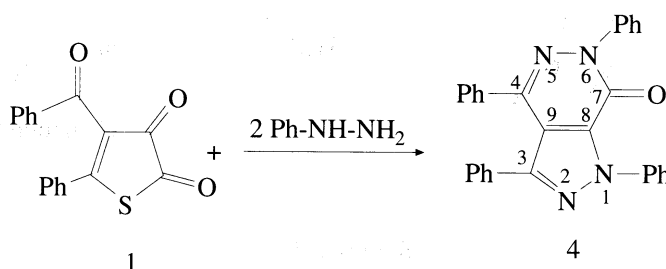
Calc.: C, 79.94; H, 4.32; N, 19.42

Found: C, 70.83; H, 4.16; N, 19.44

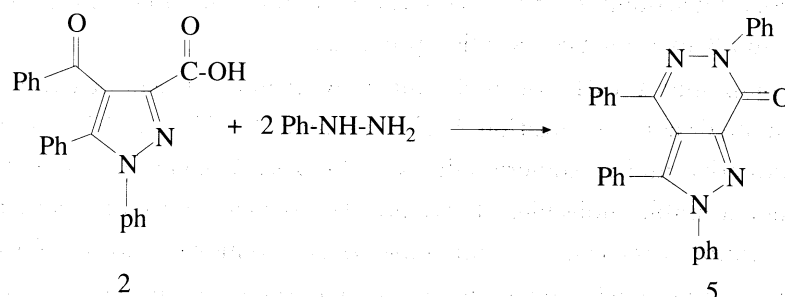
IR (KBr, cm^{-1}): 3300-2700 (N-H stretching), 1700-1640 (C=O stretching), 1260-1200 (N-N stretching).

Results and Discussion

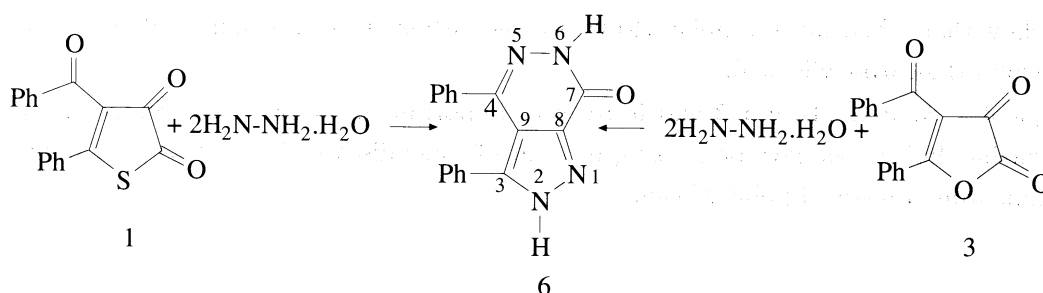
The reaction equations of **4**, **5** and **6** is given below scheme 1, scheme 2 and scheme 3.



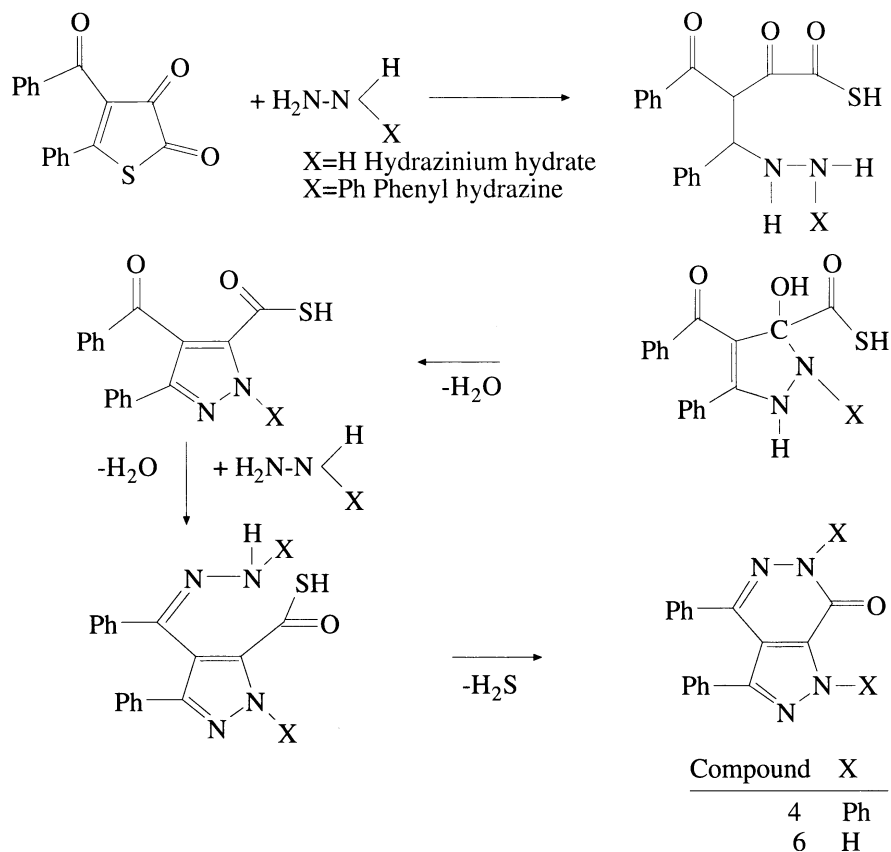
Scheme 1.



Scheme 2.



Scheme 3.



Scheme 4.

Scheme 4 shows the reaction mechanism of **4** and **6**.

Up till now, so many heterocyclic compounds were synthesized from compounds **2** and **3** with oxygenous and nitrogenous nucleophiles ^{1,2,3,4}. But the reactions with phenylhydrazine and hydrazinium hydrate of compound **2** and **3** had not been studied previously.

The reaction of compound **1** with two mole phenylhydrazine consists of two steps. First consist of attack of one mole phenylhydrazine to position 5 of compound **1**. This position is more active than the others because of the inductive and mesomeric effects. 4-benzoyl-5-phenyl-pyrazole-3- thiocarboxylic acid formed in first step is not a stable molecule. Therefore, the second molecule phenylhydrazine attack the carbon atom of benzoyl group. After this step, one mole H_2S is removed and **4** is formed.

The reaction of compound **3** with phenylhydrazine has the same mechanism as compound **1**. Here, there are two differences. First, attack of phenylhydrazine to the compound **3** results the stable molecule of 4-benzoyl-1,5-diphenyl-pyrazolo-3- carboxylic acid **2**. Second, the molecule of phenylhydrazine attacks to the carbon atom of benzoyl group and the one mole of H_2O is removed instead of H_2S . In addition, these results show that 4-benzoyl-1,5-diphenyl-pyrazolo-3- carboxylic acid is more stable than 4-benzoyl-1,5 diphenyl-pyrazolo- thiocarboxylic acid.

Consequently, compounds of **1,2** and **3** are very important in preparative organic chemistry. Some pyrazolo-pyridazine derivatives have been using to treat of some diseases ^{6,7}. These compounds **4,5** and **6** may be important from a medical point of view.

References

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