

Reactions of Cyclic Oxalyl Compounds, Part 29 [1]: A Simple Synthesis of Functionalized 1*H*-Pyrimidines**

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Summary. 4-Benzoyl-5-phenylfuran-2,3-dione (**1**) and the semicarbazones **2**, ureas and thioureas **6**, respectively, combine with loss of water and carbondioxide yielding the 1*H*-pyrimidine derivatives **3** and **7**, respectively, in moderate yields (30–75%). Hydrolysis of **3 b** leads to the 1-amino-pyrimidine-2-one **4**.

Keywords. 5-Benzoyl-1-methyleneamino-4-phenyl-1*H*-pyrimidine-2-ones; 1-Alkyl-5-benzoyl-4-phenyl-1*H*-pyrimidine-2-ones; 1,4,5-Substituted pyrimidine-2-thiones; Cyclocondensation reactions.

Reaktionen cyclischer Oxalylverbindungen, 29. Mitt. [1]: Eine einfache Synthese funktionalisierter 1*H*-Pyrimidine

Zusammenfassung. 4-Benzoyl-5-phenylfuran-2,3-dion (**1**) cyclisiert mit den Semicarbazonen **2** sowie den Harnstoffen bzw. Thioharnstoffen **6** unter Verlust von H₂O und CO₂ zu einer Reihe von 1,4,5-substituierten 1*H*-Pyrimidinen in Ausbeuten von 30–75%. Die an **3 b** exemplarisch durchgeführte Hydrolyse liefert die 1-Amino-Verbindung **4**.

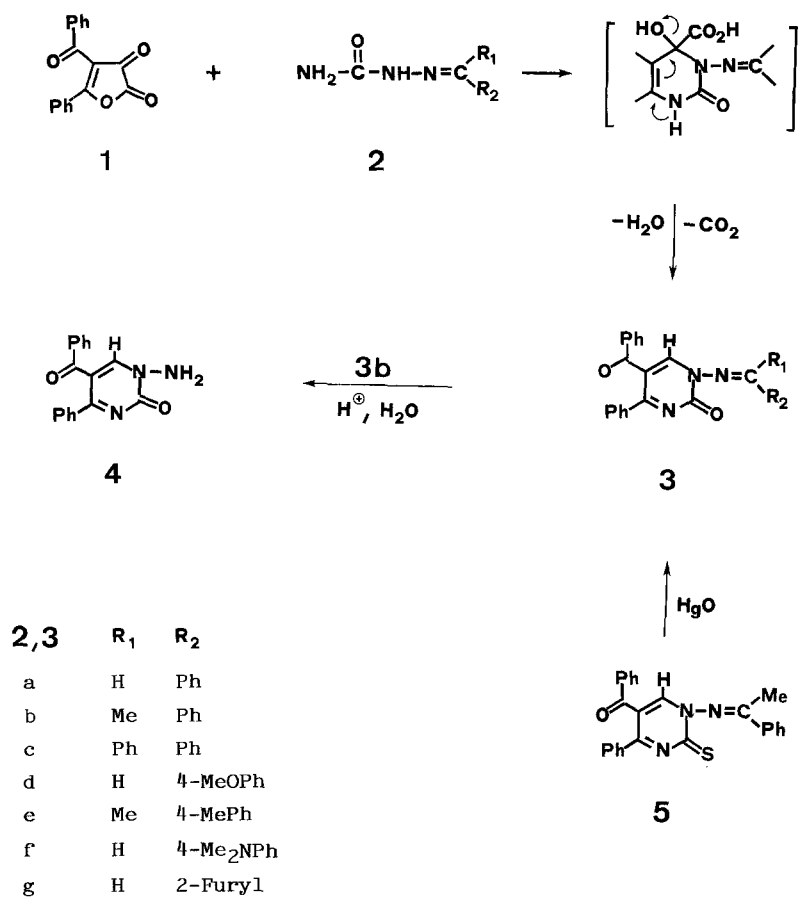
Introduction

Concerning the attempts to gain some insight into the chemical behaviour of five-membered heterocyclic 2,3-diones against NH-nucleophiles [2, 3], a convenient preparation of functionalized 1*H*-pyrimidine-2-thiones from the furan-2,3-dione **1** and several thiosemicarbazones has been reported recently [1]. Since pyrimidines in general have found much interest for biological and medicinal reasons [4], we now have extended our investigations to reactions of **1** with various semicarbazones, thioureas and ureas.

Results and Discussion

A number of 1*H*-pyrimidine-2-ones **3** were obtained in moderate yields (30–75%) from the reaction of the furandione **1** and the corresponding semicarbazones **2**. The formation of **3** obviously is proceeding via a reaction pathway quite similar to that discussed with the thiosemicarbazones [1]. It is outlined briefly in Scheme 1.

** Cordially dedicated to o. Univ.-Prof. Dr. Hans Junek on the occasion of his 60th birthday



Scheme 1

Structure elucidation of **3** is deduced mainly from elemental analysis, ir and ¹H nmr spectroscopic data (see Experimental), based on the X-ray confirmed structure of the corresponding 1*H*-pyrimidine-2-thiones [1]. In addition, the pyrimidine-2-thione **5** exemplary can be converted into the pyrimidine-2-one **3b** by desulfuration reaction with yellow HgO [5]. The structural analogy of all compounds **3** is easily seen from the ir and ¹H nmr spectra. Absorption bands at about 1 685 and 1 650 cm⁻¹, and the CH-proton of C-6, which is detected on the lower edge of the aromatic protons region at 8.0–8.5 ppm, respectively, are structural characteristics. H⁺-catalysed hydrolysis of **3b**, as an example, leads to cleavage of the C=N-double bond finally yielding the aminopyrimidine **4**. A quite similar behaviour had been found with the corresponding pyrimidine-2-thiones [1].

1,4,5-substituted 1*H*-pyrimidines **7** are obtained also from the cyclisation reaction of **1** and several ureas or thioureas respectively. Ir and ¹H nmr spectroscopic data—C=O absorption bands at about 1 650 cm⁻¹ (**7a–c**) or 1 680, 1 650 cm⁻¹ (**7d–g**) and the proton of C-6 in the region 8.2–8.8 ppm—as well as comparison with the analogues **3** and **5** [1] confirm the structural identification of **7**.

The formation of all compounds **7** should proceed again via an analogous key-intermediate and subsequent elimination of CO₂ and H₂O as described in Scheme 1.

5-Benzoyl-1-(4-methoxyphenylmethyleneamino)-4-phenyl-1H-pyrimidine-2-one (3d)

1 g **1** and 0.7 g **2d** (molar ratio 1 : 1) were heated to 115°C for 25 min (Method A); yield 0.9 g (62%), m.p. 195°C (ethanol). Ir: 1 680 s, 1 650 s (CO), 1 600 s, 1 510 m, 1 480 m cm⁻¹. ¹H nmr (CDCl₃): δ = 3.9 (s, 3 H), 6.9–7.9 (m, 14 H), 8.4 (s, 1 H at C-6), 9.5 (s, 1 H). Anal. calc. for C₂₅H₁₉N₃O₃: C 73.34, H 4.67, N 10.26; found: C 73.24, H 4.72, N 10.53.

5-Benzoyl-1-(4-methylphenyl-methylmethyleneamino)-4-phenyl-1H-pyrimidine-2-one (3e)

A mixture of 1.12 g **1** and 0.8 g **2e** (molar ratio 1 : 1) was kept at 115°C for 15 min (Method A) yielding 0.8 g (50%) **3e**, m.p. 228°C (*n*-butanol). Ir: 1 685 s, 1 640 s (CO), 1 600 s, 1 470 m cm⁻¹. ¹H nmr (CDCl₃): δ = 2.35 (s, 3 H), 2.45 (s, 3 H), 7.1–8.0 (m, 14 H), 8.1 (s, 1 H at C-6). Anal. calc. for C₂₂H₁₅N₃O₃: C 71.54, H 4.09, N 11.38; found: C 71.65, H 4.06, N 11.17.

5-Benzoyl-1-(4-dimethylaminophenyl-methyleneamino)-4-phenyl-1H-pyrimidine-2-one (3f)

Under identical reaction conditions as described for **3e** (Method A) 1.68 g **1** and 1.25 g **2f** (molar ratio 1 : 1) yield 1.4 g (55%) **3f**, m.p. 204°C (*n*-butanol). Ir: 1 680 s, 1 660 s (CO), 1 610 s, 1 590 s, 1 540 m, 1 470 m cm⁻¹. ¹H nmr (CDCl₃): δ = 3.1 (s, 6 H), 6.7–7.8 (m, 12 H), 8.4 (s, 1 H at C-6), 9.3 (s, 1 H). Anal. calc. for C₂₆H₂₂N₄O₂: C 73.92, H 5.24, N 13.26; found: C 73.87, H 5.02, N 13.04.

5-Benzoyl-1-(2-furylmethyleneamino)-4-phenyl-1H-pyrimidine-2-one (3g)

Heating of 1 g **1** and 0.56 g **2g** (molar ratio 1 : 1) in boiling benzene for 6 h (Method B) leads to isolation of 1 g (76%) of **3g**, m.p. 192°C (*n*-butanol). Ir: 1 680 s, 1 660 s (CO), 1 620 m, 1 470 s cm⁻¹. ¹H nmr (CDCl₃): δ = 6.6 (m, 1 H), 7.0–7.8 (m, 12 H), 8.4 (s, 1 H at C-6), 9.7 (s, 1 H). Anal. calc. for C₂₂H₁₅N₃O₃: C 71.54, H 4.09, N 11.38; found: C 71.65, H 4.06, N 11.17.

1-Amino-5-benzoyl-4-phenyl-1H-pyrimidine-2-one (4)

15 ml of water were added to a solution of 1 g **3b** in 5 ml of acetic acid and the mixture was then heated under reflux for 15 min. With cooling 0.37 g (50%) of **4** precipitated; m.p. 204°C (*n*-butanol). Ir: 3 300, 3 190 (NH₂), 1 680 s, 1 650 s (CO), 1 600 m, 1 480 s cm⁻¹. ¹H nmr (DMSO): 6.5 (s, 2 H, exchangeable with D₂O), 7.2–8.08 (m, 10 H), 8.5 (s, 1 H at C-6). Anal. calc. for C₁₇H₁₃N₃O₂: C 70.09, H 4.50, N 14.42; found: C 70.05, H 4.54, N 14.36.

Desulfuration of the 1H-Pyrimidine-2-thione 5

A suspension of 0.5 g yellow HgO in 10 ml dry dioxane, containing 100 mg **5** [1], was shaken at room temperature for one week. After filtration from the precipitate (HgS/HgO), treating the clear solution with charcoal and evaporation, the oily residue was dissolved in hot ethanol, with cooling finally yielding a small amount of **3b** (10 mg, 10%), identified by comparison with an authentic sample.

Synthesis of 1H-Pyrimidines 7. General Procedure

The furandione **1** and the corresponding urea or thiourea, respectively, (molar ratio 1 : 1) are refluxed in boiling benzene for 3–5 h. After evaporation the residue is crystallized from a suitable solvent (acetic acid or alcohols), in some cases previously treated with dry ether.

5-Benzoyl-1-methyl-4-phenyl-1H-pyrimidine-2-thione (7a)

From 0.28 g **1** and 0.1 g **6a** 0.185 g (60%) **7a** were obtained after 4 h reaction time; m.p. 223°C (acetic acid). Ir: 1 655 s (CO), 1 605 s, 1 500 s, 1 230 s cm⁻¹. ¹H nmr (DMSO): δ = 3.8 (s, 3 H), 7.2–8.0 (m, 10 H), 8.8 (s, 1 H at C-6). Anal. calc. for C₁₈H₁₄N₂OS: C 70.58, H 4.57, N 9.15; found: C 70.36, H 4.70, N 9.11.

5-Benzoyl-1-ethyl-4-phenyl-1H-pyrimidine-2-thione (7b)

0.23 g (72%) **7b** were isolated from reaction of 0.28 g **1** and 0.105 g **6b** and treating the oily residue with dry ether; m.p. 214°C (acetic acid). Ir: 1 650 s (CO), 1 610 s, 1 480 s, 1 440 m cm⁻¹. ¹H nmr (DMSO): δ = 1.3 (t, 3 H), 4.4 (q, 2 H), 7.2–7.9 (m, 10 H), 8.7 (s, 1 H at C-6). Anal. calc. for C₁₉H₁₆N₂OS: C 71.20, H 5.03, N 8.74; found: C 71.30, H 5.20, N 8.76.

5-Benzoyl-1,4-diphenyl-1H-pyrimidine-2-thione (7c)

An equimolar mixture of **1** and **6c** (1 mmol) was refluxed in boiling benzene for 3.5 h. After cooling the crude product precipitated and was crystallized from acetic acid yielding 0.13 g (35%) pure **7c**; m.p. 224°C. Ir: 1 660 s (CO), 1 605, 1 480 cm⁻¹. ¹H nmr (DMSO): δ = 8.2 (s, 1 H at C-6), 7.2–7.8 (m, 15 H). Anal. calc. for C₂₃H₁₆N₂OS: C 75.00, H 4.35, N 7.60, S 8.69; found: C 74.78, H 4.59, N 7.85, S 8.72.

5-Benzoyl-4-phenyl-1H-pyrimidine-2-one (7d)

An identical procedure as described with **7c** leads to the isolation of 0.1 g (36%) **7d**, m.p. 228°C (isopropanol) from the reaction of 0.28 g **1** and 0.05 g urea. Ir: 3 100 b (NH), 1 660 s (CO), 1 615 s, 1 420 s cm⁻¹. ¹H nmr (DMSO): 7.2–7.8 (m, 10 H), 8.3 (s, 1 H at C-6), 12.5 (b, 1 H).

5-Benzoyl-1-methyl-4-phenyl-1H-pyrimidine-2-one (7e)

After heating an equimolar (1 mmol) mixture of **1** and **6e** in boiling benzene for 5.5 h and evaporation, the oily residue was treated with dry ether and the crude product crystallized from *n*-butanol yielding 0.22 g (75%) **7e**, m.p. 196°C. Ir: 1 675, 1 650 s (CO), 1 620 m, 1 490 s cm⁻¹. ¹H nmr (DMSO): δ = 3.6 (s, 3 H), 7.1–7.8 (m, 10 H), 8.2 (s, 1 H at C-6).

5-Benzoyl-1-n-butyl-4-phenyl-1H-pyrimidine-2-one (7f)

Using a procedure identical with that leading to **7e**, 0.25 g (76%) **7f** were obtained from the reaction of equimolar amounts (1 mmol) **1** and **6f**; m.p. 193°C (*n*-butanol). Ir: 1 670 s, broad (CO), 1 500 s, 1 460 m cm⁻¹. ¹H nmr (CDCl₃): δ = 1.0 (t, 3 H), 1.1–2.1 (m, 4 H), 4.0 (t, 2 H), 7.1–7.8 (m, 10 H), 8.2 (s, 1 H at C-6). Anal. calc. for C₂₁H₂₀N₂O₂: C 75.88, H 6.06, N 8.43; found: C 76.06, H 5.90, N 8.30.

1-Allyl-5-benzoyl-4-phenyl-1H-pyrimidine-2-one (7g)

An equimolar mixture of **1** and **6g** was heated in boiling benzene for 3.5 h. After evaporation the crude product was purified from ethanol yielding 0.24 g (74%) **7g** (the compound crystallized with 0.5 mole of water); m.p. 157°C (ethanol). Ir: 3 550 (H₂O), 1 670 s, 1 640 s (CO), 1 490 m, 1 420 m cm⁻¹. ¹H nmr (CDCl₃): δ = 2.2 (s, H₂O), 4.6 (m, 2 H), 5.4 (m, 2 H), 6.0 (m, 1 H), 7.1–7.8 (m, 10 H), 8.2 (s, 1 H at C-6). Anal. calc. for C₂₀H₁₆N₂O₂ · 0.5 H₂O: C 73.84, H 5.23, N 8.62; found: C 73.92, H 5.34, N 8.48.

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