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Reported is the synthesis of 2-phenylfuro[3,4-*d*]pyrimidine-5,7-dione which reacts with methanol to give 5-methoxycarbonyl-2-phenyl-4-pyrimidine carboxylic acid.

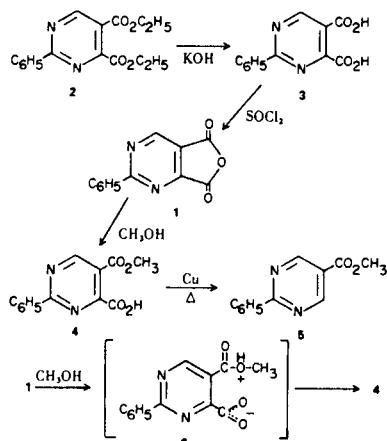
J. Heterocyclic Chem., 14, 695 (1977).

Although several furo[3,4-*d*]pyrimidines have been reported previously, apparently no reference has been made to furo[3,4-*d*]pyrimidine-5,7-diones (anhydrides of a pyrimidine-4,5-dicarboxylic acid).

The purpose of this paper is to describe the synthesis of 2-phenylfuro[3,4-*d*]pyrimidine-5,7-dione (1), its reaction with methanol, and the structure of this methanolysis product.

Alkaline hydrolysis of the diester **2** (1) gave the dicarboxylic acid **3** which had been prepared previously by another route (2). Reaction of **3** with thionyl chloride afforded the anhydride **1** which upon reaction with refluxing methanol gave a monoester-monoacid. Copper-catalyzed decarboxylation of this material resulted in the formation of an ester, the nmr spectrum of which exhibited an aromatic singlet at 9.38 δ (integral 2). This is indicative of a 5-substituted rather than a 4-substituted pyrimidine. Thus the methanolysis product has been assigned the 5-carbomethoxy-4-carboxy structure **4** which on decarboxylation formed **5**.

Hence cleavage of the anhydride **1** has occurred at the 5-acyl oxygen rather than at the 4-acyl oxygen. Although the latter mode of methanolysis might have been expected from electronic considerations, the stabilization of the intermediate carboxylate **6** by the inductive effect of the annular nitrogen might account for cleavage at the 5-acyl oxygen.



EXPERIMENTAL (3)

2-Phenyl-4,5-pyrimidinedicarboxylic acid (3).

A mixture of 120 g. (0.40 mole) of **2** (1) and 800 ml. of 10% potassium hydroxide was stirred and refluxed for 16 hours. The hot solution was diluted with 500 ml. water, acidified with concentrated hydrochloric acid, and stirred at ambient temperatures for 1.5 hours. The solid was filtered, washed with 2 x 150 ml. of water, and dried to give 96 g. (98%) of the product, m.p. 279-281°. Dissolution in 5% potassium hydroxide, filtration, and subsequent acidification with 5% hydrochloric acid gave the analytical sample, m.p. 282-284°, lit. m.p. 279-281° (2); nmr (DMSO-*d*₆) δ : 7.60-7.68 (m, 3, aromatic C-H); 8.41-8.51 (m, 2, aromatic C-H); 9.41 (s, 1, C₆-H); ir μ : 5.83, 5.93 (C=O); 6.38 (C=C).

Anal. Calcd. for C₁₂H₈N₂O₄: C, 59.02; H, 3.30; N, 11.47. Found: C, 58.94; H, 3.24; N, 11.47.

2-Phenylfuro[3,4-*d*]pyrimidine-5,7-dione (1).

A mixture of 36.6 g. (0.15 mole) of **3** and 250 ml. of thionyl chloride was stirred and refluxed for 2 hours. Upon standing at ambient temperatures for 15 hours, the clear solution deposited 25.4 g. (75%) of the product. The analytical sample, m.p. 188-191°, was obtained by recrystallization from toluene; nmr (DMSO-*d*₆) δ : 7.58-7.75 (m, 3, aromatic C-H); 8.41-8.58 (m, 2, aromatic C-H); 9.41 (s, 1, C₆-H) ir μ : 5.35, 5.55 (C=O), 6.20, 6.28, 6.38 (C=C).

Anal. Calcd. for C₁₂H₆N₂O₃: C, 63.72; H, 2.67; N, 12.39. Found: C, 63.52; H, 2.72; N, 12.28.

5-Methoxycarbonyl-2-phenyl-4-pyrimidinecarboxylic Acid (4).

To 500 ml. methanol stirred at 20° was added quickly 33.7 g. (0.15 mole) of **1**. The mixture was stirred and refluxed for 3 hours, then cooled and stirred for 15 minutes in an ice bath. The solid was filtered, washed with 2 x 50 ml. of methanol, and dried to give 29.6 g. (76%) of the product, m.p. 226-229°. Recrystallization from methanol gave the analytical sample, m.p. 228-229°; nmr (DMSO-*d*₆) δ : 4.02 (s, 3, CH₃); 7.50-7.77 (m, 3, aromatic C-H); 8.41-8.58 (m, 2, aromatic C-H); 9.40 (s, 1, C₆-H); ir μ : 5.68 (C=O, ester); 5.83 (C=O, acid); 6.33, 6.48 (C=C); 7.70-7.90 (C-O-C ester).

Anal. Calcd. for C₁₃H₁₀N₂O₄: C, 60.46; H, 3.90; N, 10.85. Found: C, 60.26; H, 3.90; N, 10.83.

Methyl 2-Phenyl-5-pyrimidinecarboxylate (5).

A mixture of 38.5 g. (0.15 mole) of **4** and 4.5 g. of copper powder (Fischer-Electrolytic purified) was heated at 250-275° for 45 minutes, cooled, and extracted with 4 x 150 ml. of boiling acetone. The combined extracts were decolorized and concentrated to dryness *in vacuo* to give the crude product. Recrystallization from 1600 ml. of methanol gave 12.8 g. (38%) of the ester, m.p. 156-160°. Further recrystallization from methanol gave the analytical sample, m.p. 161-163°; nmr (deuteriochloroform) δ : 3.98 (s, 3, CH₃); 7.45-7.63 (m, 3, aromatic C-H); 8.46-8.65 (m, 2, aromatic C-H); 9.38 (s, 2, C₄-H, C₆-H); ir μ : 5.80 (C=O, ester); 6.30, 6.50 (C=C);

7.70-7.80 (C-¹³C ester).

Anal. Calcd. for C₁₂H₁₀N₂O₂: C, 67.28; H, 4.71; N, 13.08.
Found: C, 67.15; H, 4.69; N, 13.11.

REFERENCES AND NOTES

(1) S. Yurugi, M. Hieda, T. Fushimi, T. Kawamatsu, H. Sugihara and M. Tomimoto, *Chem. Pharm. Bull.*, **20**, 1513 (1972).

(2) R. A. Clarke, B. Graham, and B. E. Christensen, *J. Am. Chem. Soc.*, **70**, 1088 (1948).

(3) Melting points were taken in a Mel Temp apparatus in open capillary tubes and are uncorrected. The nuclear magnetic resonance spectra were taken on a Varian A-60A instrument and were compared with TMS as an internal standard. Infrared spectra were determined as Nujol Mulls on a Perkin-Elmer 137B spectrophotometer.