A one-step synthesis of 5,7-diaryl-1,5-dihydro (or 1,2,3,5-tetrahydro)-pyrano [2,3-d]pyrimidin-2,4-diones (or 2-thioxo-4-ones)


*Department of Chemistry, University of Dhaka, Dhaka 1000, Bangladesh
and
Department of Natural Science, American International University-Bangladesh (AIUB), Banani, Dhaka 1213, Bangladesh
E-mail: mgahmed1@gmail.com

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A one-step synthesis of 5,7-diaryl-1,5-dihydro-pyrano[2,3-d]pyrimidin-2,4-diones, 3a-c and 5,7-diaryl-2-thioxo-1,2,3,5-tetrahydropyrano[2,3-d]pyrimidin-4-ones, 3d-g has been achieved by the cyclocondensation of barbituric acid or thiobarbituric acid in glacial acetic acid in the presence of phosphorous pentoxide. The structures of the compounds 3a-g have been determined by their UV, IR, $^1$H NMR, $^{13}$C NMR, mass spectral data and elemental analyses.

The synthesis of pyranopyrimidines has been a field of continued interest because of their pharmacological activities. Although a variety of routes for the synthesis of these compounds have been described, the majority of them involve several steps and the yields are poor. Therefore, it was felt necessary to develop an efficient method for the synthesis of these compounds relatively in good yields. There is a report on the reactions of barbituric acids with $\alpha,\beta$-unsaturated carbonyl systems.

In continuation to our previous work on the synthesis of 5,7-diaryl-1,5-dihydropyrano[2,3-d]pyrimidin-2,4-diones, we now report the synthesis of 5,7-diaryl-1,5-dihydropyrano[2,3-d]pyrimidin-2,4-diones, 3a-c and 5,7-diaryl-2-thioxo-1,2,3,5-tetrahydropyrano[2,3-d]pyrimidin-4-ones, 3d-g which have been characterized by spectroscopic methods and elemental analyses. These compounds were hitherto not reported in the literature.

The formation of compounds 3a-g may be explained by the initial formation of a 1:1 adduct (A) followed by cyclocondensation (Scheme I). The formation of such an adduct has been reported in the literature.

Note

Compound 1 (Z=O) reacted with 1-(4-chlorophenyl)-3-phenyl-2-propen-1-one 2a to give a yellow crystalline solid 3a at refluxing temperature in glacial acetic acid in the presence of phosphorous pentoxide. Its mass spectrum, gave a peak at $m/z$ 353.12 (M$^+$). The $^1$H NMR spectrum of compound 3a showed besides other usual signals, two singlets at $\delta$ 10.92 (NH, 1H, 1-H) and 6.05 (NH, 1H, 1-H), one broad-singlet at $\delta$ 5.97 (1H, 6-H) and another broad-singlet at $\delta$ 4.34 (1H, 5-H). Its $^{13}$C NMR showed signals at $\delta$ 174.16 (4-C), 161.46 (9-C), 154.27 (7-C), 145.35 (2-C), 104.02 (6-C), 93.02 (10-C) and 35.19 (5-C). On the basis of these spectral data it was assigned the structure 7-(4-chloro-phenyl)-5-phenyl-1,5-dihydropyra-no[2,3-d]pyrimidine-2,4-dione, 3a. Similarly 1 (Z=O or S) in reaction with other arylideneacetophenones 2b-d afforded the compounds (3b-g, Scheme I). The structures of all these compounds were assigned on the basis of their spectral data and elemental analyses.

Experimental Section

The UV spectra were run in methanol using Shimadzu UV-160A ultraviolet spectrophotometer. Melting points are uncorrected. IR spectra were recorded as KBr pellet using Shimadzu IR-470 infrared spectrophotometer in the range of 4000-400 cm$^{-1}$. $^1$H NMR spectra were run in DMSO on a Bruker 400 MHz NMR spectrometer using TMS as internal standard. $^{13}$C NMR spectra were run in DMSO and mass spectra in JEOL JMS-HX 110A spectrophotometer. All the compounds gave expected C, H and N analyses.

A mixture of arylideneacetophenone (0.005 mol) and barbituric acid or thiobarbituric acid (0.005 mol)
were dissolved in acetic acid (10 mL) and P_2O_5 (2 g) in a round-bottomed flask equipped with a magnetic stirrer, a refluxing condenser and a drying tube. The reaction mixture was refluxed at 120°C for 15 hr and the course of the reaction was followed by TLC on silica gel plates (eluting solvent: EtOAc if not otherwise mentioned). The mixture was allowed to cool and treated with crushed ice. The solid thus obtained was filtered off, washed with cold water, dried and purified by recrystallization from ethanol.

7-(4-Chloro-phenyl)-5-phenyl-1,5-dihydropyrano[2,3-d]pyrimidine-2,4-dione, 3a: Light yellow solid; Yield 14%; m.p. 304-06°C; R_f 0.48; UV (ε): 284 nm (3072) (π→π* of C=O); IR: 3420, 3100 (OH, NH), 1680, 1525 (C=O), 1440, 1415, 1350, 1280, 1260, 1200, 1180, 1100 cm\(^{-1}\); \(^1\)H NMR: δ 10.92 (s, 1H, NH, 3-H), 8.06-7.16 (m, 9H, aromatic protons), 6.05 (s, 1H, NH, 1-H), 5.97 (bs, 1H, 6-H), 4.34 (bs, 1H, 5-H); \(^1^3\)C NMR: δ 174.16 (4-C), 161.46 (9-C), 154.27 (7-C), 145.35 (2-C), 144.10-124.57 (aromatic carbons), 104.02 (6-C), 93.02 (10-C), 35.19 (5-C); MS: m/z 353.12 (M\(^+\)), 289.1, 165.1, 154.1 (100%), 107.0, 65.0; Anal. Found: C, 68.25; H, 3.67; N, 7.86; Calcd. for C\(_{19}\)H\(_{13}\)N\(_2\)O\(_2\)Cl: C, 64.68; H, 3.69; N, 7.94%.

5-Phenyl-7-p-tolyl-1,5-dihydropyrano[2,3-d]pyrimidine-2,4-dione, 3b: Light brown solid; Yield 36%; m.p. 272-73°C; R_f 0.34; UV (ε): 284 nm (3213) (π→π* of C=O); IR: 3450, 3200 (OH, NH), 1690, 1520 (C=O), 1440, 1350, 1210, 1180, 1120 cm\(^{-1}\); \(^1\)H NMR: δ 10.92 (s, 1H, NH, 3-H), 8.09-7.20 (m, 9H, aromatic protons), 6.10 (s, 1H, NH, 1-H), 5.86 (d, J = 5.2, 1H, 6-H), 4.47 (bs, 1H, 5-H); 2.26 (s, 3H, Ar-CH\(_3\)); \(^1^3\)C NMR: δ 164.10 (4-C), 153.30 (9-C), 149.50 (7-C), 145.10 (2-C), 135.10-124.10 (aromatic carbons), 103.20 (6-C), 87.30 (10-C), 35.40 (5-C), 22.65 (Ar-CH\(_3\)); MS: m/z 332.21 (M\(^+\)), 332.2, 307.2, 255.2, 154.1 (100%), 136.1, 79.0; Anal. Found: C, 69.43; H, 4.87; N, 8.13; Calcd. for C\(_{20}\)H\(_{16}\)N\(_2\)O\(_2\): C, 72.29; H, 4.82; N, 8.43%.

7-(4-Methoxy-phenyl)-5-phenyl-1,5-dihydropyrano[2,3-d]pyrimidine-2,4-dione, 3c: Orange solid; Yield 6%; m.p. 240-41°C; R_f 0.75; UV (ε): 292 nm (7348) (π→π* of C=O); IR: 3320, 3150 (OH, NH), 1680, 1505 (C=O), 1440, 1345, 1295, 1270, 1200, 1180, 1110 cm\(^{-1}\); \(^1\)H NMR: δ 10.91 (s, 1H, NH, 3-H), 7.60 (d, J = 7.32, 2H, H-2´ and 6´), 7.27-7.18 (m, 5H, rest of aromatic protons), 6.97 (d, J = 7.66, 2H, H-3´ and 5´), 5.85 (s, 1H, NH, 1-H), 5.71 (bs, 1H, 6-H), 4.42 (bs, 1H, 5-H), 3.78 (s, 3H, Ar-OCH\(_3\)); \(^1^3\)C NMR: δ 163.29 (4-C), 159.52 (9-C), 154.43 (7-C), 149.67 (2-C), 144.98-114.00 (aromatic carbons), 102.42 (6-C), 87.55 (10-C), 55.26 (Ar-OCH\(_3\)), 34.97 (5-C); MS: m/z 348.17 (M\(^+\)), 349.2 (100%), 271.1, 217.2, 135.1, 77.0, 23.0; Anal. Found: C, 67.02; H, 4.82; N, 7.35; Calcd. for C\(_{20}\)H\(_{18}\)N\(_2\)O\(_3\): C, 68.96; H, 4.60; N, 8.05%.

5,7-Diphenyl-2-thioxo-1,2,3,5-tetrahydropyranono[2,3-d]pyrimidin-4-one, 3d: Brown solid; Yield 09%; m.p. 284-86°C; R_f 0.23(CHCl\(_3\)); UV (ε): 288 nm (11717) (π→π* of C=O); IR: 3430 (OH, NH), 1665, 1620 (C=O), 1440, 1360, 1260, 1215, 1180, 1130 cm\(^{-1}\); \(^1\)H NMR: δ 12.35 (s, 1H, NH, 3-H), 7.69-7.20 (m, 10H, aromatic protons), 6.03 (s, 1H, NH, 1-H), 5.70 (bs, 1H, 6-H), 4.47 (bs, 1H, 5-H); \(^1^3\)C NMR: δ 161.46 (4-C), 154.27 (9-C), 145.35 (7-C), 174.16 (2-C), 144.19-124.57 (aromatic carbons), 104.49 (6-C), 93.02 (10-C), 35.19 (5-C); MS: m/z 336.10 (M\(^+\)), 335.1 (100%), 257.1, 154.1, 136.1, 89.0; Anal. Found:
C, 67.76; H, 4.32; N, 8.23; Calcd. for C₁₉H₁₄N₂O₂S: C, 67.86; H, 4.77; N, 8.33%.

7-(4-Chlorophenyl)-5-phenyl-2-thioxo-1,2,3,5-tetrahydropyrrano[2,3-d]pyrimidin-4-one, 3e: Light brown solid; Yield 11%; m.p. 300-02°C; Rf 0.46; UV (ε): 294 nm (9170) (π→π* of C=O); IR: 3450, 3100 (OH, NH), 1665, 1620, 1550 (C=O), 1358, 1258, 1240, 1218, 1180, 1130 cm⁻¹; ¹H NMR: δ 12.30 (s, 1H, NH, 3-H), 4.06-7.13 (m, 9H, aromatic protons), 6.10 (s, 1H, NH, 1-H), 5.96 (d, J = 5.2, 1H, 6-H), 4.34 (bs, 1H, 5-H); ¹³C NMR: δ 168.18 (4-C), 165.90 (9-C), 152.27 (7-C), 183.30 (2-C), 144.00-127.05 (aromatic carbons), 103.08 (6-C), 88.20 (10-C), 35.57 (5-C); MS: m/z 366 (M⁺), 231, 216, 222, 146, 134, 128, 119 (100%), 103, 102; Anal. Found: C, 61.92; H, 3.64; N, 7.32; Calcd. for C₁₉H₁₄N₂O₂SCl: C, 61.87; H, 3.53; N, 7.60%.

5-Phenyl-2-thioxo-7-p-tolyl-1,2,3,5-tetrahydropyrrano[2,3-d]pyrimidin-4-one, 3f: Grey solid; Yield 20%; m.p. 300-02°C; Rf 0.23 (CHCl₃); UV (ε): 287 nm (2926) (π→π* of C=O); IR: 3400 (OH, NH), 1665, 1620, 1550 (C=O), 1410, 1355, 1260, 1235, 1215, 1180, 1115 cm⁻¹; ¹H NMR: δ 12.93 (s, 1H, NH, 3-H), 7.79-7.26 (m, 9H, aromatic protons), 6.15 (s, 1H, NH, 1-H), 5.91 (bs, 1H, 6-H), 4.47 (bs, 1H, 5-H), 2.68 (s, 3H, Ar-CH₃); ¹³C NMR: δ 160.98 (4-C), 153.58 (9-C), 145.07 (7-C), 173.79 (2-C), 138.82-124.13 (aromatic carbons), 103.10 (6-C), 92.57 (10-C), 34.97 (5-C), 20.78 (Ar-CH₃); MS: m/z 348.16 (M⁺)(100%), 271.1, 154.1, 136.1, 91.0, 57.1; Anal. Found: C, 68.19; H, 4.65; N, 7.96; Calcd. for C₂₀H₁₆N₂O₂S: C, 68.96; H, 4.59; N, 8.05%.

7-(4-Methoxyphenyl)-5-phenyl-2-thioxo-1,2,3,5-tetrahydropyrrano[2,3-d]pyrimidin-4-one, 3g: Light orange solid; Yield 11%; m.p. 269-71°C; Rf 0.78; UV (ε): 288 nm (11717) (π→π* of C=O); IR: 3450, 3100 (OH, NH), 1665, 1620, 1540 (C=O), 1450, 1410, 1355, 1300, 1250, 1210 cm⁻¹; ¹H NMR: δ 12.33 (s, 1H, NH, 3-H), 7.62 (d, J = 7.42, 2H, H-2′ and 6′) 7.26-7.19 (m, 5H, rest of aromatic protons) 6.95 (d, J = 7.56, 2H, H-3′ and 5′), 5.83 (s, 1H, NH, 1-H), 5.69 (bs, 1H, 6-H), 4.47 (bs, 1H, 5-H), 3.76 (s, 3H, Ar-CH₃); ¹³C NMR: δ 160.25 (4-C), 154.16 (9-C), 145.18 (7-C), 173.99 (2-C), 144.26-114.28 (aromatic carbons), 102.27 (6-C), 92.95 (10-C), 55.54 (Ar-CH₃), 34.99 (5-C); MS: m/z 364.14 (M⁺), 365.1 (100%), 287.1, 154.1, 136.1, 89.0, 57.1; Anal. Found: C, 65.81; H, 4.41; N, 7.74; Calcd. for C₂₀H₁₆N₂O₂S: C, 65.93; H, 4.40; N, 7.69%.

References