An Expeditious Synthesis of 6-Amido-(1H,3H)-Pyrimidine-2,4-Diones from Uracil-6-Carboxylic Acid

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ABSTRACT: 2,4-Dichloro pyrimidine-6-carbonylchloride (2) was synthesized by refluxing uracil-6-carboxylic acid (orotic acid) with phosphorus oxychloride and phosphorus pentachloride. Compound (2) underwent a smooth coupling reaction with a number of substituted arylamines to yield 2, 4-dichloro-6-amidopyrimidines (8-12) which were converted to the corresponding 2, 4-dimethoxy-6-amidopyrimidines (13-17) on treatment with sodium methoxide in methanol. Compounds 13-17 afforded 6-amido-(1H, 3H)-pyrimidine-2, 4-diones (18-22) in good yield on refluxing with 6 M hydrochloric acid. These pyrimidinone derivatives may exhibit antiviral actitities.

Key word: Pyrimidine, uracil, orotic acid, phosphorus oxychloride, arylamines, antiviral

INTRODUCTION

The importance of 5-substituted derivatives of uracil as anticancer and antiviral agents is well-established. 5-Flourouracil(1) (5-FU) I and the corresponding 2-deoxyribonucleoside (FuD) are being used as anticancer agents whereas 5-ido-2-deoxyuridine(2) is of importance as an antiviral agent. Dihydroalkoxybenzyloxopyrimidines (DABOs) II are a new class of specific inhibitors of human immunodeficiency virus type 1 (HIV-1) which possess a benzyl moiety and an alkyl (cycloalkyl) chain linked through an oxygen bridge to the uracil or thymine base. Replacement of the side chain oxygen with sulfur atom furnished thio-DABOs, which showed increased anti-HIV activity. Miyasaka et al have reported that 1-[(2-hydroxyethoxy)methyl]-6-phenylthio) thymine (HEPT) III has potent and selective in vitro activity against HIV-1.

The synthesis and antiviral activities of a series of 6-arylmethyl-1-allyloxyxymethyl)-5-alkyluracil derivatives have been reported. Recently, we have reported a synthesis of 4-acyl-2, 6-dioxo-1, 2, 3, 6-tetrahydropyrimidines (6-arylacurcils and 4-acyl-6-aryl-2-oxo-2, 3-dihydropyrimidines. In view of the significant biological activities of various 6-substituted uracils and related pyrimidine derivatives we became interested in developing methods for the synthesis of novel 6-substituted uracils.

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pyrimidines. In this paper we report a very facile method for the synthesis of a number of 6-amidopyrimidine-2,4-diones from orotic acid.

MATERIALS AND METHODS

Melting points were determined in open capillary tubes on Gallenkamp (England) melting point apparatus and were uncorrected. IR spectra were recorded on a Shimadzu FTIR spectrophotometer and UV spectra were recorded in dry EtOH with a Shimadzu visible spectrophotometer. $^1$H NMR and $^{13}$C NMR spectra were recorded on a Bruker DPX - 400 spectrophotometer (400 MHz) using tetramethylsilane as internal reference. Analytical thin-layer chromatography (TLC) was performed on precoated silica gel 60 F$_{254}$ (E. Merck), and the spots were visualized with UV light. Column chromatography was performed on silica gel (60-120 mesh). Elemental analyses (C, H, N) were carried out on a Perkin Elmer 240 C analyser. Orotic acid, POCl$_3$, primary arylamine, and other reagents were purchased from E. Merck (Germany) and Fluka (Switzerland).

Preparation of 2,4-dichloropyrimidine-6-carbonyl chloride (2). A mixture of 2,4-dioxo-1,3,5-trihydro pyrimidine-6-carboxylic acid (Orotic acid) 5.0 g (0.032 mol) and phosphorus oxychloride (POCl$_3$, 40 ml) was refluxed for 24 hours at 105-108 °C, then phosphorus pentachloride (15 g, 0.072 mol) was added into the reaction mixture. The mixture was again refluxed for 24 hours. Phosphorus oxychloride was removed under reduced pressure. The residue was distilled under reduced pressure and 2,4-dichloropyrimidine-6-carbonyl chloride (2) (4.0 g) was obtained as dense colorless liquid. An analytical sample was prepared by redistillation of the product, b.p.108-109 °C (5.0 mm) [Lit$^{17}$ 109 °C (5.0 mm)]. Anal. Calcd. For C$_7$H$_3$Cl$_2$OCl$_3$: 28.40; N, 13.24; Cl, 50.43. Found: C, 28.25; N, 13.35; Cl, 50.23.

Synthesis of 2,4-dichloro-6-substituted phenylamido pyrimidines (8-12). The substituted anilines 3-7 were dissolved in benzene and added to the cold solution of 2,4-dichloropyrimidine-6-carbonyl chloride (5.0g, 23.64 mmol) drop wise. The mixture was then allowed to warm up to room temperature and stirred at room temperature (25°C) for 2 hours. The mixture was kept at 0-5°C for overnight. Then the mixture was concentrated by evaporation of benzene under reduced pressure, washed with distilled water (100 ml) followed by saturated aqueous solution of sodium hydrogen carbonate (2 x 50 ml) and extracted with chloroform (3 x 50 ml). The combined organic layer was washed with distilled water (2 x 25 ml), dried over anhydrous Na$_2$SO$_4$, filtered, and concentrated under reduced pressure. The crude products were purified by column chromatography and crystallized from methanol to afford the desired products (8-12).

2,4-dichloro-6-p-methoxyphenylamido pyrimidine (8). Yellowish amorphous powder, yield: 5.85 g (82%), mp 147-149 °C; UV (EtOH): $\lambda_{\max }$ 352.00 nm; IR (KBr): $\nu_{\max }$ 3354.0, 1689.5, 1564.2, 1529.4, 1508.2, 1415.7, 1298.0, 1253.6, 1250.0, 1033.8, 829.3 & 788.8 cm$^{-1}$. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 3.83 (3H, s, Ar-CH$_3$), 6.94 (2H, d, $J$ = 9.02 Hz, Ar-H), 7.65 (2H, d, $J$ = 9.00, Ar-H), 8.17 (1H, s, H-5), 9.42 (s, -NH-); $^{13}$C NMR 100 MHz, CDCl$_3$): $\delta$ = 54.50, 55.15 & 55.54 (-OCH$_3$), 100.39 (Ur-CH), 114.34, 121.51 (Ar-CH), 130.38, 133.09 (Ar-C), 156.80, 159.22, 159.97 (Ur-C), 165.13 (C=O). Anal. Calcd for C$_{12}$H$_7$Cl$_2$N$_2$O$_2$: C, 48.34; H, 3.04; N, 14.09. Found: C, 47.40; H, 3.22; N, 13.65.

2,4-dichloro-6-p-chlorophenylamido pyrimidine (9). Reddish fine crystal yield 6.07 g, (85%), mp 166-167°C; UV (EtOH): $\lambda_{\max }$ 306.00 nm; IR (KBr): $\nu_{\max }$ 3359.8, 1685.7, 1566.1, 1527.5, 1488.9, 1400.2, 1247.9, 837.0, & 758.0 cm$^{-1}$. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.36 (2H, d, $J$ = 8.2 Hz, Ar-H), 7.68 (2H, d, $J$ = 8.14 Hz, Ar-H), 8.14 (1H, s, H-5), 9.49 (s, -NH-); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 118.16 (Ur-CH), 119.01, 119.89, 124.43, 126.57 (Ar-CH), 130.06, 131.21 (Ar-C), 157.90, 159.19, 160.02 (Ur-C), 165.41 (C=O); Anal. Calcd for C$_{11}$H$_7$Cl$_2$N$_2$O: C, 43.67; H, 2.00; N, 13.89. Found: C, 43.81; H, 2.15; N, 13.85.

2,4-dichloro-6-m-chlorophenylamido pyrimidine (10). Reddish amorphous powder, yield: 5.93 g (83%), mp 160-162 °C; UV (EtOH): $\lambda_{\max }$ 324.00 nm;
IR (KBr): ν max 3340.5, 1695.3, 1593.1, 1525.6, 1251.7 & 680.8 cm⁻¹; 1H NMR (400 MHz, CDCl₃): δ = 7.20 (1H, d, J = 7.22 Hz, Ar-H), 7.33 (1H, t, J = 8.08 Hz, Ar-H), 7.58 (1H, d, J = 8.16 Hz, Ar-H), 7.86 (s, Ar-H) 8.16 (1H, s, H-5), 9.50 (s, -NH-); 13C NMR (100MHz, CDCl₃): δ = 118.61 (Ur-CH), 118.36, 120.28, 125.71, 130.29 (Ar-CH), 135.06, 137.53 (Ar-C), 157.96, 159.89, 160.02 (Ur-C), 165.41 (C=O).

Anal. Calcd for C₁₁H₁₃N₃O: C, 43.67; H, 2.00; N, 13.89. Found: C, 43.90; H, 2.23; N, 13.75.

2,4-dichloro-6-m-methylphenylamido pyrimidine (11). Off white crystal, yield: 5.53 g (83%), mp 159-161 °C; UV (EtOH): λ max 320.00 nm; IR (KBr): ν max 3369.4, 1687.6, 1566.1, 1525.6, 1317.3, 1294.1, 1245.9 & 825.5 cm⁻¹; 1H NMR (400 MHz, CDCl₃): δ = 2.34 (3H, s, Ar-CH₃), 7.18 (2H, d, J = 8.28 Hz, Ar-H), 7.59 (2H, d, J = 8.32 Hz, Ar-H), 8.14 (s, 1H, H-5), 9.43 (s, -NH-); 13C NMR (100MHz, CDCl₃): δ = 20.96 (Ar-CH₃), 118.22 (Ur-CH), 120.06, 129.75 (Ar-CH₃), 133.89, 135.39 (Ar-C), 157.60, 159.81, 160.46 (Ur-C), 165.13 (C=O). Anal. Calcd for C₁₁H₁₁Cl₂N₂O: C, 51.09; H, 3.22; N, 14.89. Found: C, 50.98; H, 3.28; N, 14.88.

2,4-Dichloro-6-m-methylphenylamido pyrimidine (12). Reddish crystal, yield: 5.46 g (82%), mp 147-149 °C; UV (EtOH): λ max 356.00 nm; IR (KBr): ν max 3355.9, 3068.7, 1687.6, 1531.4, 1488.9, 1309.6, 1296.1, 1247.9 & 794.6 cm⁻¹; 1H NMR (400 MHz, CDCl₃): δ = 2.41 (3H, s), 7.06 (1H, d, J = 7.43 Hz, Ar-H), 7.31 (1H, q, J = 7.61 Hz, Ar-H), 7.58 (2H, d, J = 9.42, Ar-H) 8.18 (s, 1H, H-5), 9.46 (s, -NH-); 13C NMR (100MHz, CDCl₃): δ = 21.49 (Ar-CH₃), 117.28 (Ur-C), 118.29, 120.74, 126.46, 129.12 (Ar-CH₃), 136.34, 139.32 (Ar-C), 157.75, 159.91, 160.47 (Ur-C), 165.25 (C=O). Anal. Calcd for C₁₂H₁₀Cl₂N₂O: C, 51.09; H, 3.22; N, 14.89. Found: C, 50.88; H, 3.26; N, 14.76.

General procedure for the synthesis of 2,4-dimethoxy-6-substituted phenylamido pyrimidines (13-17). 2,4-Dichloro-6-substituted phenylamido pyrimidines (8-12) (1mmol) were added separately to the cold solution of sodium methoxide solution prepared by dissolving sodium (3 mmol) in methanol (30 ml). The mixture was refluxed at 60°C for 4 hours under Nitrogen atmosphere. After removal of solvent the crude mass was neutralized with dilute hydrochloric acid and extracted with chloroform (3x50 mL). The combined chloroform layer was washed with distilled water (2x25 mL), dried over anhyd NaSO₄, filtered, and concentrated under reduced pressure. The residues were crystallized from methanol to obtain the desired products (13-17).

2,4-dimethoxy-6-p-methoxyphenylamido pyrimidine (13). Off white amorphous powder, yield: 3.34 g (82%), mp 112-113°C; UV (EtOH): λ max 286.00 nm; IR (KBr): ν max 3328.2, 3003.0, 2947.0, 1685.7, 1589.2, 1573.8, 1535.2, 1514.0, 1483.2, 1465.8, 1384.8, 1355.9, 1315.4, 1301.9, 1263.3, 1232.4, 1218.9, 1201.6, 1186.1, 1186.1, 1126.4, 1076.2 1043.4, 987.5, 933.5 & 769.5 cm⁻¹; 1H NMR (400 MHz, CDCl₃): δ = 3.79 (3H, s, Ar-OCH₃), 4.03 (3H, s, Ar-OCH₃), 4.08 (3H, s, Ar-OCH₃), 6.90 (1H, d, J = 8.98 Hz, Ar-H), 7.25 (1H, s, H-5), 7.64 (1H, d, J = 8.98, Ar-H) 9.54 (s, -NH-); 13C NMR (100MHz, CDCl₃): δ = 54.50 (Ar-CH₂), 55.15, 55.54 (Ur-OCH₃), 100.39 (Ur-CH), 130.38, 133.09 (Ar-CH), 156.80, 159.22, 159.97 (Ur-C), 165.13 (C=O). Anal. Calcd for C₁₄H₁₄Cl₂N₂O₃: C, 58.13; H, 5.23; N, 14.53. Found: C, 58.00; H, 5.26; N, 14.76.

2,4-dimethoxy-6-p-chlorophenylamido pyrimidine (14). White amorphous powder, yield: 3.39 g (86%), mp 118-120 °C; UV (EtOH): λ max 282.00 nm; IR (KBr): ν max 3355.9, 3107.1, 1691.5, 1606.6, 1583.4, 1569.9, 1519.8, 1492.8, 1460.0, 1415.7, 1398.3, 1382.9, 1303.8, 1286.4, 1238.2, 1197.7, 1093.6, 1024.1, 983.6 & 829.3 cm⁻¹; 1H NMR (400 MHz, CDCl₃): δ = 4.02 (3H, s, Ar-OCH₃), 4.06 (3H, s, Ar-OCH₃), 7.22 (1H, s, H-5), 7.31 (2H, d, J = 8.78 Hz, Ar-H), 7.65 (2H, d, J = 8.8 Hz, Ar-H), 9.63 (s, -NH-); 13C NMR (100MHz, CDCl₃): δ = 54.56 (Ur-OCH₃), 55.17 (Ur-OCH₃), 100.50 (Ur-CH), 118.83, 119.89, 124.43, 126.57 (Ar-CH₃), 131.06, 131.22 (Ar-C), 145.29, 150.81, 151.81 (Ur-C), 164.03 (C=O). Anal. Calcd for C₁₃H₁₂Cl₂N₂O₂: C, 53.16; H, 4.12; N, 14.31. Found: C, 52.91; H, 4.11; N, 14.33.

2,4-dimethoxy-6-m-chlorophenylamido pyrimidine (15). Light pink amorphous powder, yield: 3.86 g (87%), mp 120-121°C; UV (EtOH): λ max
276.00 nm; IR (KBr): 𝜈_{max} 3355.9, 3105.2, 1706.9, 1610.5, 1598.9, 1569.9, 1580.2, 1481.2, 1475.4, 1419.5, 1396.4, 1367.4, 1290.3, 1263.3, 1201.6, 1188.1 & 1112.9 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 4.05 (3H, s, Ar-CH₃), 4.09 (3H, s, Ar-CH₃), 7.14 (1H, d, J = 7.80 Hz, Ar-H) 7.28 (1H, dd, J = 8.03, 7.78 Hz, Ar-H), 7.55 (1H, d, J = 8.01 Hz, Ar-H), 7.85 (1H, d, J = 8.04 Hz, Ar-H), 8.32 (Ar-CH), 10.55, 164.81 (Ar-C), 173.42 (C=O). Anal. Calcd for C₁₁H₁₂N₃O₃: C, 61.53; H, 5.53; N, 15.38. Found: C, 61.23; H, 5.62; N, 15.65.

**General procedure for the synthesis 6-arylamido pyrimidine-2,4-diones (18-22).** The demethylation reaction of 2,4-dimethoxy-6-substituted phenylamido pyrimidines 13-17 were performed separately by refluxing with 6 M hydrochloric acid aqueous solution for 4-6 hours. The reaction mixture was cooled and amorphous powder was separated by filtration, washed with chilled water, dried and crystallized from ethanol to afford 6-substituted phenylamido uracils 18-22 in good yield.

6-ₚ-methoxyphenylamido pyrimidine-2,4-dione (18). White amorphous powder, yield: 1.96 g (87%), mp 276-277 °C; UV (EtOH): 𝜈_{max} 2380.0 nm; IR (KBr): 𝜈_{max} 3296.1,3016.5, 1735.8, 1660.6, 1618.2,1508.3, 1440.7, 837.0 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆): δ = 3.74 (3H, s, Ar-CH₃), 6.17 (1H, s, H-5), 6.95 (2H, d, J = 8.96 Hz, Ar-H), 7.59 (2H, d, J = 8.96 Hz, Ar-H), 10.40 (1H, s, Ar-NH), 10.87 (1H, s, Ar-NH), 11.29 (s,1H, -NH); ¹³C NMR (100 MHz, DMSO-d₆): δ = 55.21 (Ar-CH₂), 100.21 (Ar-CH), 113.93, 121.98 (Ar-CH₂), 130.75, 145.67 (Ar-C), 150.79, 156.20, 158.39 (Ar-C), 164.09 (-C=O); DEPT-135: 55.21 (Ar-CH₂), 100.21 (Ar-CH), 113.93, 121.98 (Ar-CH₂); Anal. Calcd for C₁₁₄H₁₃N₃O₃: C, 55.17; H, 4.24; N, 16.09. Found: C, 55.00; H, 4.15; N, 16.10.

6-ₚ-chlorophenylamidopyrimidine-2,4-dione (19). White amorphous powder, yield: 1.91 g (88%), mp 281-283 °C; UV (EtOH): 𝜈_{max} 3560.00 nm; IR (KBr): 𝜈_{max} 3296.2, 3095.5, 2829.4, 1735.8, 1660.6, 1596.9, 1529.4, 1498.6, 1440.7, 837.0 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆): δ = 6.18 (s,H, H-5), 7.44 (d, 1H, J = 8.83 Hz, Ar-H), 7.71 (d, 2H, J = 8.85 Hz, Ar-H), 10.64 (s, 1H, Ar-NH), 10.95 (s, 1H, Ar-NH), 11.32 (s, 1H, -NH); ¹³C NMR (100 MHz, DMSO-d₆): δ = 100.71 (Ar-CH₁), 118.83, 119.89, 124.43, 130.57 (Ar-CH₂), 133.06, 139.22 (Ar-C), 145.29, 150.81, 159.81 (Ar-C), 164.03 (C=O). Anal. Calcd for C₁₁₄H₁₃N₃O₃: C, 49.73; H, 3.04; N, 15.82. Found: C, 49.92; H, 3.28; N, 15.53.

6-ₚ-chlorophenylamidopyrimidine-2,4-dione (20). White amorphous powder, yield: 1.69 g (85%),
After usual workup the 1H,21.14 ety was found to react under reduced pressure and 1pyrimidines Hz, 24 20.49 (Ar he 1H, max 1H, max 2.30 (s, t, d, J = 7.89 Hz, Ar-H), 7.41(1H, t, J = 8.1 Hz, Ar-H), 7.61 (1H, d, J = 8.37 Hz, Ar-H), 7.85 (1H, s, Ar-H), 10.67 (1H, s, Ar-NH), 10.97 (1H, s, Ur-NH), 11.34 (s, -NH); 13C NMR (400 MHz, DMSO-d6): δ = 100.71 (Ar-CH), 118.83, 119.89, 124.43, 130.57 Ar-CH), 133.06, 139.22 (Ar-C), 145.29, 150.81, 159.19 (Ur-C), 164.03 (C=O). DEPT-135: δC 100.71 (Ar-CH), 118.82, 119.82, 124.43, 130.56 (Ar-CH).

6-p-methylphenylamido pyrimidine-2,4-dione (21). White amorphous powder, yield: 1.97 g (88), mp 267-269 °C; UV (EtOH): λmax 328.00 nm; IR (KBr): vmax 3280.5, 3014.5, 1735.4, 1616.2, 1505.8, 1488.4, 1265.6, 1110.6 & 802.3 cm⁻¹; 1H NMR (400 MHz, DMSO-d6): δ = 2.30 (3H, s, Ar-CH₃), 5.67 (1H, s, H-5), 6.68 (2H, d, J = 8.18 Hz, Ar-H), 7.06 (d, 2H, J = 8.20 Hz, Ar-H), 9.94 (1H, s, Ur-NH), 10.39 (1H, s, Ur-NH), 10.80 (1H, s, -NH); 13C NMR (100 MHz, DMSO-d6): δ = 20.49 (Ar-CH₃), 100.33 (Ar-CH), 120.41, 129.19 (Ar-CH), 133.82, 135.24 (Ar-C), 145.66, 150.81, 158.65 (Ar-C), 164.10 (-C=O). DEPT-135: δC 20.49 (Ar-CH₃), 100.33(Ar-CH), 120.41, 129.19(Ar-CH); Anal. Calcd for C₁₂H₁₁N₃O₂: C, 58.77; H, 4.52; N, 17.13. Found: C, 58.60; H, 4.68; N, 16.87.

6-m-methylphenylamido pyrimidine-2,4-dione (22). White amorphous powder, yield: 1.90 g (85%), mp 262-264°C; UV (EtOH): λmax 242.00 nm; IR(KBr): v max 3157.3, 2925.8, 1712.7, 1614.3, 1560.3, 1488.8, 1369.5, 1266.2, 1113.8, 1020.2 cm⁻¹; 1H NMR (400 MHz, DMSO-d6): δ = 2.30 (s, 3H, Ar-CH₃), 6.17 (s, 1H, H-5), 6.98 (d, 1H, J = 7.5 Hz, Ar-H), 7.25 ((1H, t, J = 7.83 Hz, Ar-H), 7.47 (1H, d, J = 8.31 Hz, Ar-H), 7.52 (1H, s, Ar-H), 10.44 (1H, s, Ur-NH), 10.91 (1H, s, Ur-NH), 11.31 (1H, s, -NH); 13C NMR (100 MHz, DMSO-d6): δ = 21.14 (Ar-CH₃), 100.41 (Ar-CH), 117.61, 120.92, 125.29, 128.65 (Ar-CH), 137, 138.06 (Ar-C), 145.62, 150.84, 158.81 (Ur-C), 164.11 (C=O).

RESULTS AND DISCUSSION

It has been reported a very facile method for the synthesis of a number of 6-amidopyrimidine-2,4-diones from orotic acid. 2,4- Dichloropyrimidine-6-carbonyl chloride (2) was synthesized according to the procedure of Gershon [10] by heating Orotic acid 1 with phosphorus oxychloride and phosphorus pentachloride as shown in the scheme 1. Phosphorus oxychloride was recovered under reduced pressure. The residue was distilled under reduced pressure and 2,4-dichloropyrimidine-6-carbonyl chloride (2) (4.0 g) was obtained as dense colorless liquid.

The compound 2,4-dichloropyrimidine-6-carbonyl chloride 2 underwent a smooth reaction with a number of substituted amine derivatives in which the acid chloride moiety was found to react predominantly to produce desired product 2,4-dichloro-6-substituted phenylamido pyrimidines (8-12) as shown in the Scheme-1.

2,4-dichloro-6-substituted phenylamidopyrimidines (8-12) were converted to the corresponding dimethoxy pyrimidines (13-17) on treatment with sodium methoxide in methanol as shown in the scheme 1 and Table 1. After usual workup the residues were crystallized from methanol and 2,4-dimethoxy-6-substituted phenylamidopyrimidines (13-17) were obtained in good yield (82-87%). The demethylation reaction of 2,4-dimethoxy-6-substituted phenylamido pyrimidines (13-17) were performed by heating with 6 M hydrochloric acid aqueous solution for 4-6 hours and 6-substituted phenylamido uracils (18-22) were obtained in good yield (85-88%) after usual workup as shown in the scheme 1 and Table 1. The compounds (18-22) were crystallized from ethanol.

In conclusion, a convenient and facile method is developed for the synthesis of 6-amido pyrimidine-2,4-diones from orotic (uracil-6-carboxylic acid) acid. The purification of the synthesized compounds were very simple, mainly crystallization. A variety of functional groups can be introduced at the C-6 positions of the pyrimidine ring by this procedure. It is believed that the synthesized pyrimidine derivatives might show antiviral activity as reported in literature. We are planning to test our compound against virus.
Table 1. Synthesis of 2,4-dichloro-6-substituted phenylamidopyrimidines (8-12); 2,4-dimethoxy-6-arylamido pyrimidines (13-17); 6-arylamido pyrimidine-2,4-diones (18-22)

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<th>2,4-Dimethoxy-6-arylamido pyrimidine&lt;sup&gt;b&lt;/sup&gt; (13-17)</th>
<th>6-arylamido pyrimidine-2,4-dione&lt;sup&gt;c&lt;/sup&gt; (18-22)</th>
<th>Yield%&lt;sup&gt;d&lt;/sup&gt;</th>
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<sup>a</sup>Yield% based on 2,4-dichloropyrimidine-6-carbonyl chloride 2; <sup>b</sup>Yield% based on 2,4-dichloro-6-substituted phenylamido pyrimidines (8-12); <sup>c</sup>Yield% based on 2,4-dimethoxy-6-substituted arylamido pyrimidines (13-17);<sup>d</sup>Yield% based on 2,4-dimethoxy-6-substituted arylamido pyrimidines (13-17)
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