Studies on Pyrimidine-Annelated Heterocycles: Synthesis of Pyrrolo[3,2-*d*]pyrimidines by Amine Oxide Rearrangement

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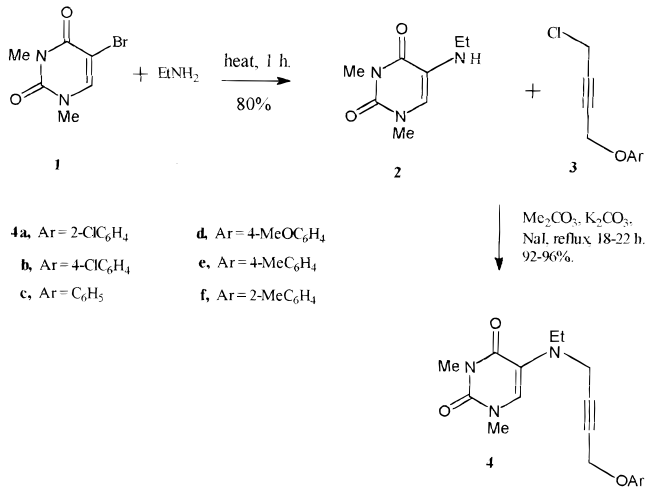
A number of pyrrolo[3,2-*d*]pyrimidine derivatives (**5a**−**f**) were synthesized in 90−95% yields from the corresponding 5-[*N*-[4-(aryloxy)but-2-ynyl]-*N*-ethylamino]-1,3-dimethyluracils **4a**−**f** by simple treatment with 1 equiv of *m*-chloroperoxybenzoic acid in dichloromethane at 0−5 °C for 12−15 h. The resulting benzoates (**5a**−**f**) were easily converted to methoxy derivatives **11a**−**f** in 92−94% yields when refluxed in methanol for 20−22 h.

Introduction

The importance of pyrimidine and its derivatives is well-known.[1,2] Numerous pyrimidine and uracil-based molecules,[3] e.g., 3′-azido-3′-deoxythymidine (AZT), 2′,3′-dideoxycytidine (DDC), (*E*)-5-[2-(bromovinyl)-2′-deoxyuridine] (BVDU), active against cancer and AIDS viruses,[4] have already been synthesized. Functionalization of uracils at the C-5 and C-6 positions leads to biologically interesting molecules but it is not a simple task; it requires rather sophisticated and tedious reaction conditions.[5] 6-Substituted uracils have been recently found to be active against HIV and other viruses.[6] [3,3] Sigmatropic rearrangement is an excellent method for C−C bond formation. We have recently reported facile formation of furo[3,2-*d*]pyrimidines and pyrano[3,2-*d*]-pyrimidines in excellent yields from the corresponding 5-(propargyloxy)uracils. Amine oxide rearrangement is an excellent method[7] for C−C bond formation as well as the construction of the pyrrole ring in fused heterocycles. This is a very mild and simple method affording fused pyrroles in almost quantitative yields. This prompted us to undertake a study on the synthesis of pyrrolo[3,2-*d*]pyrimidine derivatives by the application of sigmatropic rearrangements of suitably substituted amine oxides. We now report the results of this investigation.

Scheme 1



The starting materials for this study, 5-[*N*-[4-(aryloxy-)but-2-ynyl]-*N*-ethylamino]-1,3-dimethyluracils were prepared in 92−96% yields by the reaction of 1,3-dimethyl-5-(*N*-ethylamino)uracil (**2**) with different 1-(aryloxy)-4-chlorobut-2-ynes (**3**) in refluxing acetone in the presence of anhydrous potassium carbonate for 20−22 h. 1,3-Dimethyl-5-(*N*-ethylamino)uracil (**2**) in turn was prepared in 80% yield from 5-bromo-1,3-dimethyluracil (**1**) by heating with excess aqueous ethylamine (40%) on a water bath for 1 h (Scheme 1).

Results and Discussion

Substrates **4a**−**f** contain a propargylamine moiety. As our aim was to use sigmatropic rearrangement for the formation of the C−C single bond at the C-6 position of

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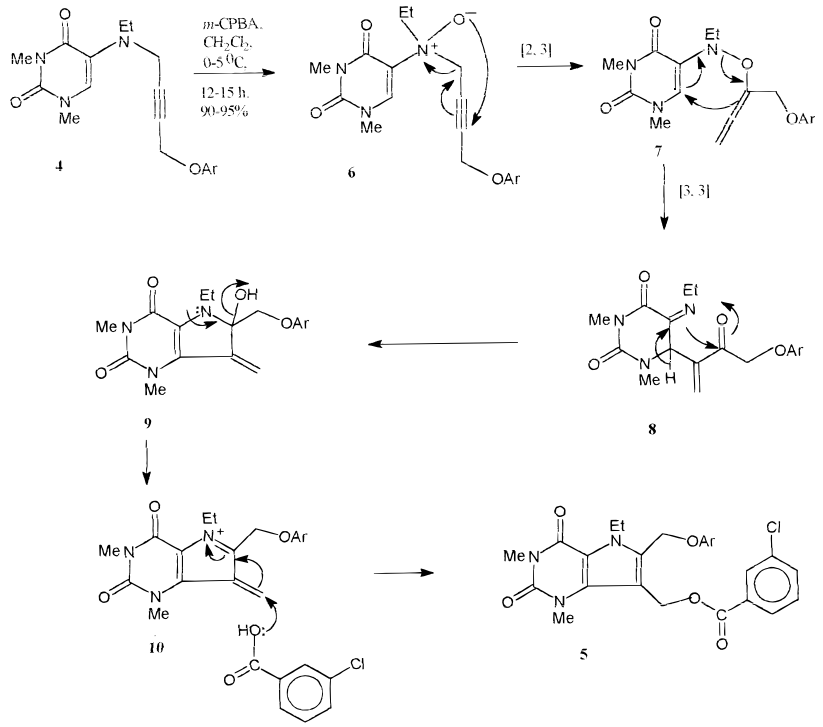
Scheme 2

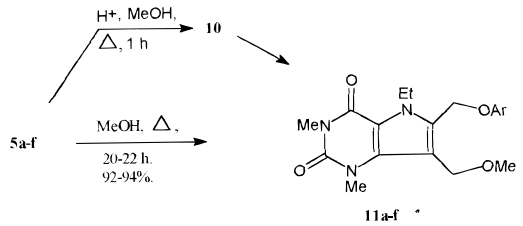


the uracils **4a**−**f**, we considered the well-known amine oxide rearrangement methodology for the construction of fused pyrrole rings. This was shown to be an excellent one-step process, and the fused pyrroles were obtained in almost quantitive yields simply by stirring a solution of the arylpropargylamine in dichloromethane at room temparature with 1 equiv of *m*-chloroperoxybenzoic acid (*m*-CPBA). We therefore decided to find whether the five-membered pyrrole ring with a 5,6-double bond in the uracil moiety could be constructed via the aforesaid amine oxide rearrangement. Consequently, the tertiary amine **4a** was treated with 1 equiv of *m*-chloroperoxybenzoic acid in dichloromethane at ambient temperature to provide pyrrolopyrimidine derivative **5a** as a sole isolable compound (95%, mp 150 °C). Thus, all the remaining substrates **4b**−**f** have also been similarly treated to furnish the corresponding pyrrolopyrimidine derivatives **5b**−**f** (Scheme 2).

The formation of the pyrrolopyrimidine derivatives **5** from **4** is easily explicable[8] by the formation of the *N*-oxide **6** followed by a [2,3]-sigmatropic rearrangement[9] to give the intermediate **7**, which subsequently undergoes a [3,3]-sigmatropic rearrangement[10] and ketolization to give ketol **9**. Presumably, intermediate **9** first loses water in acid-catalyzed elimination to give iminium ion **10**, which is then added to benzoic acid (a poor nucleophile) (Scheme 2).

The *m*-chlorobenzoate group of the pyrrolopyrimidine derivatives **5a**−**f** is easily replaced by a methoxy group by refluxing compounds **5a**−**f** in absolute methanol for 20−22 h to give a series of methoxy derivatives **11a**−**f** (Scheme 3). This can be achieved in 1 h if catalytic amount of hydrochloric acid is added to the reaction mixture.

Scheme 3



In conclusion, this is an extremely facile and mild synthesis of pyrrolo[3,2-*d*]pyrimidine derivatives. The generality of the method has been demonstrated by the successful conversion of six substrates **4a**−**f** into pyrrolopyrimidine derivatives **5a**−**f** in excellent yields. These materials have the potential to be useful as drugs. The methodology described here seems to be the simplest one for the synthesis of these compounds.

Experimental Section

Melting points are uncorrected. UV absorption spectra were recorded in EtOH. IR spectra were run for KBr disks. ^{1}H NMR spectra were determined for solutions in $CDCl_3$ with TMS as internal standard. Elemental analyses and recording of mass spectra [JEOL D-300 (EI)] were carried out at RSIC (CDRI), Lucknow. Silica gel (60−120 mesh) was used for chromatographic separation. Petroleum ether refers to the fraction boiling between 60 and 80 °C.

Preparation of 1,3-Dimethyl-5-(ethylamino)uracil (2). A mixture of 5-bromo-1,3-dimethyluracil (11.0 g, 50 mmol) and 40% aqueous $EtNH_2$ (50 mL) was refluxed on a water bath for 1 h. The reaction mixture was evaporated to dryness, and the residue was extracted with $CHCl_3$ (3 × 25 mL). The $CHCl_3$ extract was washed with water and dried (Na_2SO_4). The solvent was removed to give a solid that was recrystallized from $CHCl_3$−petroleum ether.

1,3-Dimethyl-5-(ethylamino)uracil (2): yield 80%; mp 102 °C; λ_{max} (log ϵ) 240 (2.90), 312 (2.83) nm; IR (KBr) ν_{max} 3350, 1690, 1660, 1630 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.28 (t, J = 10.5 Hz, 3H), 2.91 (q, J = 10.5 Hz, 2H), 3.37 (s,

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3H), 3.38 (s, 3H), 6.06 (s, 1H), 6.80 (s, 1H); MS *m/z* 183 (M^+). Anal. Calcd for $C_8H_{13}N_3O_2$: C, 52.45; H, 7.10; N, 22.95. Found: C, 52.55; H, 7.17; N, 23.02.

Preparation of 1-(Aryloxy)-4-chlorobut-2-yne. These compounds were prepared according to published procedures.[7a,e,f]

General Procedure for the Synthesis of Compounds 4a−f. A mixture of 1-(aryloxy)-4-chlorobut-2-yne (4 mmol), 1,3-dimethyl-5-(ethylamino)uracil (0.732 g, 4 mmol), anhyd K_2CO_3 (3 g), and NaI (0.05 g) was refluxed in dry Me_2CO (75 mL) for 18−22 h. The solvent was removed, and the residual solid was subjected to column chromatography over silica gel. The products **4a−f** were obtained as viscous liquids when the column was eluted with benzene−ethyl acetate (3:1).

5-[*N*-[4-(2′-Chlorophenoxy)but-2-ynyl]-*N*-ethylamino]-1,3-dimethyluracil (4a): yield 96%; liquid; λ_{max} (log ϵ) 223 (3.34), 275 (2.95) nm; IR (KBr) ν_{max} 1690, 1640 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 1.08 (t, J = 7.5 Hz, 3H), 2.94 (q, J = 7.5 Hz, 2H), 3.28 (s, 3H), 3.34 (s, 3H), 3.96 (t, J = 1.5 Hz, 2H), 4.8 (t, J = 1.5 Hz, 2H), 6.68 (s, 1H), 6.88−7.44 (m, 4H); MS *m/z* 363, 361 (M^+). Anal. Calcd for $C_{18}H_{20}ClN_3O_3$: C, 59.75; H, 5.53; N, 11.61. Found: C, 59.83; H, 5.65; N, 11.71.

5-[*N*-[4-(4′-Chlorophenoxy)but-2-ynyl]-*N*-ethylamino]-1,3-dimethyluracil (4b): yield 92%; liquid; λ_{max} (log ϵ) 226 (3.36), 275 (2.80) nm; IR (KBr) ν_{max} 1695, 1640 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 1.08 (t, J = 7.5 Hz, 3H), 2.94 (q, J = 7.5 Hz, 2H), 3.28 (s, 3H), 3.34 (s, 3H), 3.96 (t, J = 1.5 Hz, 2H), 4.68 (t, J = 1.5 Hz, 2H), 6.66 (s, 1H), 6.82−6.98 (dt, J = 8.5, 1.5 Hz, 2H), 7.18−7.32 (dt, J = 8.5, 1.5 Hz, 2H); MS *m/z* 363, 361 (M^+). Anal. Calcd for $C_{18}H_{20}ClN_3O_3$: C, 59.75; H, 5.53; N, 11.61. Found: C, 59.87; H, 5.55; N, 11.77.

1,3-Dimethyl-5-[*N*-(4-phenoxybut-2-ynyl)-*N*-ethylamino]uracil (4c): yield 93%; liquid; λ_{max} (log ϵ) 223 (3.40), 297 (2.97) nm; IR (KBr) ν_{max} 1685, 1635, 1210 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 1.08 (t, J = 7.5 Hz, 3H), 2.94 (q, J = 7.5 Hz, 2H), 3.2 (s, 3H), 3.32 (s, 3H), 3.96 (t, J = 1.5 Hz, 2H), 4.7 (t, J = 1.5 Hz, 2H), 6.64 (s, 1H), 6.92−7.40 (m, 5H); MS *m/z* 327 (M^+). Anal. Calcd for $C_{18}H_{21}N_3O_3$: C, 66.05; H, 6.42; N, 12.84. Found: C, 66.15; H, 6.53; N, 12.92.

1,3-Dimethyl-5-[*N*-[4-(4′-methoxyphenoxy)but-2-ynyl]-*N*-ethylamino]uracil (4d): yield 93%; liquid; λ_{max} (log ϵ) 226 (3.40), 290 (3.06) nm; IR (KBr) ν_{max} 1685, 1630 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 1.08 (t, J = 7.5 Hz, 3H), 2.94 (q, J = 7.5 Hz, 2H), 3.24 (s, 3H), 3.32 (s, 3H), 3.78 (s, 3H), 3.96 (t, J = 1.5 Hz, 2H), 4.65 (t, J = 1.5 Hz, 2H), 6.68 (s, 1H), 6.84−6.88 (m, 4H); MS *m/z* 357 (M^+). Anal. Calcd for $C_{19}H_{23}N_3O_4$: C, 63.86; H, 6.44; N, 11.76. Found: C, 63.92; H, 6.55; N, 11.79.

1,3-Dimethyl-5-[*N*-[4-(4′-methylphenoxy)but-2-ynyl]-*N*-ethylamino]uracil (4e): yield 94%; liquid; λ_{max} (log ϵ) 223 (3.24), 297 (2.76) nm; IR (KBr) ν_{max} 1685, 1635 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 1.08 (t, J = 7.5 Hz, 3H), 2.28 (s, 3H), 2.94 (q, J = 7.5 Hz, 2H), 3.2 (s, 3H), 3.34 (s, 3H), 3.96 (t, J = 1.5 Hz, 2H), 4.72 (t, J = 1.5 Hz, 2H), 6.64 (s, 1H), 6.8−7.4 (m, 4H); MS *m/z* 341 (M^+). Anal. Calcd for $C_{19}H_{23}N_3O_3$: C, 66.86; H, 6.74; N, 12.31. Found: C, 66.95; H, 6.77; N, 12.44.

1,3-Dimethyl-5-[*N*-[4-(2′-methylphenoxy)but-2-ynyl]-*N*-ethylamino]uracil (4f): yield 95%; liquid; λ_{max} (log ϵ) 223 (3.07), 297 (2.67) nm; IR (KBr) ν_{max} 1690, 1640, cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 1.08 (t, J = 7.5 Hz, 3H), 2.22 (s, 3H), 2.94 (q, J = 7.5 Hz, 2H), 3.2 (s, 3H), 3.34 (s, 3H), 3.96 (t, J = 1.5 Hz, 2H), 4.72 (t, J = 1.5 Hz, 2H), 6.64 (s, 1H), 6.82−7.4 (m, 4H); MS *m/z* 341 (M^+). Anal. Calcd for $C_{19}H_{23}N_3O_3$: C, 66.86; H, 6.74; N, 12.31. Found: C, 66.99; H, 6.69; N, 12.42.

General Procedure for the Synthesis of Compounds 5a−f. A solution of *m*-chloroperbenzoic acid (0.35 g, 1 mmol) in CH_2Cl_2 (20 mL) was added dropwise to a well-stirred solution of **4a−f** (1 mmol) in CH_2Cl_2 (20 mL) at 0−5 °C during 15 min. The mixture was stirred for an additional 12−15 h at room temperature. The reaction mixture was then successively washed with 10% aqueous Na_2CO_3 (3 × 50 mL) and water (3 × 50 mL) and dried (Na_2SO_4). The solvent was evaporated to give a crude residue that was purified by chromatography over silica gel, eluted with benzene−ethyl acetate (9:1). All the products **5a−f** were recrystallized from $CHCl_3$−petroleum ether.

7-[[(3′-Chlorobenzoyl)oxy]methyl]-6-[(2′-chlorophenoxy)methyl]-1,3-dimethyl-5-ethylpyrrolo[3,2-*d*]pyrimidine-2,4-dione (5a): yield 95%; mp 150 °C; λ_{max} (log ϵ) 224 (3.16), 273 (2.72) nm; IR (KBr) ν_{max} 1715, 1690, 1650 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.45 (t, J = 7.5 Hz, 3H), 3.44 (s, 3H), 3.81 (s, 3H), 4.49 (q, J = 7.5 Hz, 2H), 5.30 (s, 2H), 5.50 (s, 2H), 7.36−7.46 (m, 6H), 7.86−7.92 (m, 2H); MS *m/z* 520, 516 (M^+). Anal. Calcd for $C_{25}H_{23}Cl_2N_3O_5$: C, 58.13; H, 4.45; N, 8.13. Found: C, 58.19; H, 4.55; N, 8.33.

7-[[(3′-Chlorobenzoyl)oxy]methyl]-6-[(4′-chlorophenoxy)methyl]-1,3-dimethyl-5-ethylpyrrolo[3,2-*d*]pyrimidine-2,4-dione (5b): yield 90%; mp 160 °C; λ_{max} (log ϵ) 228 (3.62), 273 (3.19) nm; IR (KBr) ν_{max} 1710, 1690, 1640 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.43 (t, J = 7.5 Hz, 3H), 3.44 (s, 3H), 3.81 (s, 3H), 4.49 (q, J = 7.5 Hz, 2H), 5.21 (s, 2H), 5.48 (s, 2H), 6.95 (dt, J = 8.5, 1.5 Hz, 2H), 7.36 (q, J = 7.5 Hz, 4H), 7.54 (d, J = 7.8 Hz, 1H), 7.86 (d, J = 7.8 Hz, 1H); MS *m/z* 520, 516 (M^+). Anal. Calcd for $C_{25}H_{23}Cl_2N_3O_5$: C, 58.13; H, 4.45; N, 8.13. Found: C, 58.23; H, 4.56; N, 8.27.

7-[[(3′-Chlorobenzoyl)oxy]methyl]-1,3-dimethyl-5-ethyl-6-(phenoxymethyl)pyrrolo[3,2-*d*]pyrimidine-2,4-dione (5c): yield 91%; mp 145 °C; λ_{max} (log ϵ) 225 (3.60), 272 (3.20) nm; IR (KBr) ν_{max} 1710, 1685, 1645 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.45 (t, J = 7.5 Hz, 3H), 3.45 (s, 3H) 3.80 (s, 3H), 4.51 (q, J = 7.5 Hz, 2H), 5.23 (s, 2H), 5.49 (s, 2H), 7.03 (t, J = 7.5 Hz, 3H), 7.36 (q, J = 7.5 Hz, 4H) 7.54 (d, J = 7.8 Hz, 1H), 7.86 (d, J = 7.8 Hz, 1H); MS *m/z* 483, 481 (M^+). Anal. Calcd for $C_{25}H_{24}ClN_3O_5$: C, 62.30; H, 4.98; N, 8.72. Found: C, 62.44; H, 5.10; N, 8.83.

7-[[(3′-Chlorobenzoyl)oxy]methyl]-1,3-dimethyl-5-ethyl-6-[(4′-methoxyphenoxy)methyl]pyrrolo[3,2-*d*]pyrimidine-2,4-dione (5d): yield 94%; mp 174 °C; λ_{max} (log ϵ) 226 (3.48), 267 (2.98) nm; IR (KBr) ν_{max} 1705, 1680, 1640 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.44 (t, J = 7.5 Hz, 3H), 3.44 (s, 3H), 3.76 (s, 3H), 3.79 (s, 3H), 4.51 (q, J = 7.5 Hz, 2H), 5.16 (s, 2H), 5.46 (s, 2H), 6.86−6.92 (m, 4H), 7.36 (t, J = 7.5 Hz, 1H), 7.48−7.56 (m, 1H), 7.87 (d, J = 1.5 Hz, 1H), 7.94 (t, J = 1.5 Hz, 1H); MS *m/z* 513, 511 (M^+). Anal. Calcd for $C_{26}H_{26}ClN_3O_6$: C, 60.99; H, 5.08; N, 8.21. Found: C, 61.05; H, 5.19; N, 8.33.

7-[[(3′-Chlorobenzoyl)oxy]methyl]-1,3-dimethyl-5-ethyl-6-[(4′-methylphenoxy)methyl]pyrrolo[3,2-*d*]pyrimidine-2,4-dione (5e): yield 94%; mp 151 °C; λ_{max} (log ϵ) 224 (3.65), 274 (3.26) nm; IR (KBr) ν_{max} 1710, 1690, 1640 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.45 (t, J = 10.5 Hz, 3H), 2.29 (s, 3H), 3.42 (s, 3H), 3.71 (s, 3H), 4.49 (q, J = 10.5 Hz, 2H), 5.17 (s, 2H), 5.45 (s, 2H), 6.80−6.86 (m, 2H), 6.96−7.20 (m, 2 H), 7.26−7.38 (m, 1H), 7.48−7.54 (m, 1H), 7.84−7.90 (m, 1H); MS *m/z* 497, 495 (M^+). Anal. Calcd for $C_{26}H_{26}ClN_3O_5$: C, 62.96; H, 5.24; N, 8.47. Found: C, 62.77; H, 5.31; N, 8.33.

7-[[(3′-Chlorobenzoyl)oxy]methyl]-1,3-dimethyl-5-ethyl-6-[(2′-methylphenoxy)methyl]pyrrolo[3,2-*d*]pyrimidine-2,4-dione (5f): yield 94%; mp 138 °C; λ_{max} (log ϵ) 225 (3.51), 273 (3.19) nm; IR (KBr) ν_{max} 1710, 1685, 1640 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.44 (t, J = 10.5 Hz, 3H), 2.13 (s, 3H), 3.42 (s, 3H), 3.80 (s, 3H), 4.53 (q, J = 10.5 Hz, 2H), 5.20 (s, 2H), 5.45 (s, 2H), 6.90−6.96 (m, 2H), 7.48−7.52 (m, 1 H), 7.84−7.88 (m, 2H); MS *m/z* 497, 495 (M^+). Anal. Calcd for $C_{26}H_{26}ClN_3O_5$: C, 62.96; H, 5.24; N, 8.47. Found: C, 62.99; H, 5.35; N, 8.45.

General Procedure for the Synthesis of Compound 11a−f. The benzoates **5a−f** (0.5 mmol) in dry methanol (25 mL) were refluxed on a water bath for 20−22 h. Methanol was removed, and the residual mass was extracted with $CHCl_3$. The $CHCl_3$ solution was then washed with 5% aqueous Na_2CO_3 (3 × 25 mL) and water (3 × 10 mL) and dried over Na_2SO_4. The solvent was removed to give a crude residue that was purified by chromatography over silica gel. Compounds **11a−f** were obtained when the column was eluted with benzene−ethyl acetate (3:1). All the products **11a−f** were recrystallized from $CHCl_3$−petroleum ether. This was achieved in 1 h when one drop of HCl was added to the compound **5** (0.1 mmol) in MeOH (5 mL).

6-[(2′-Chlorophenoxy)methyl]-1,3-dimethyl-5-ethyl-7-(methoxymethyl)pyrrolo[3,2-*d*]pyrimidine-2,4-dione (11a): yield 94%; mp 188 °C; λ_{max} (log ϵ) 224 (3.01), 273 (2.69)

nm; IR (KBr) ν_{max} 1680, 1645 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.45 (t, J = 7.5 Hz, 3H), 3.38 (s, 3H), 3.44 (s, 3H), 3.76 (s, 3H), 4.49 (q, J = 7.5 Hz, 4H), 5.1 (s, 2H), 7.10−7.24 (m, 2H), 7.42−7.46 (m, 2H); MS m/z 393, 391 (M^+). Anal. Calcd for $C_{19}H_{22}ClN_3O_4$: C, 58.23; H, 5.61; N, 10.72. Found: C, 58.29; H, 5.77; N, 10.77.

6-[(4′-Chlorophenoxy)methyl]-1,3-dimethyl-5-ethyl-7-(methoxymethyl)pyrrolo[3,2-*d*]pyrimidine-2,4-dione (11b): yield 92%; mp 182 °C; λ_{max} (log ϵ) 228 (3.50), 272 (3.18) nm; IR (KBr) ν_{max} 1685, 1640 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.40 (t, J = 7.5 Hz, 3H), 3.38 (s, 3H), 3.43 (s, 3H), 3.73 (s, 3H), 4.46 (q, J = 7.5 Hz, 4H), 5.01 (s, 2H), 6.90−6.96 (m, 2H), 7.26−7.30 (m, 2H); MS m/z 393, 391 (M^+). Anal. Calcd for $C_{19}H_{22}ClN_3O_4$: C, 58.23; H, 5.61; N, 10.72. Found: C, 58.33; H, 5.66; N, 10.88.

1,3-Dimethyl-5-ethyl-7-(methoxymethyl)-6-(phenoxymethyl)pyrrolo[3,2-*d*]pyrimidine-2,4-dione (11c): yield 93%; mp 138 °C; λ_{max} (log ϵ) 224 (2.97), 270 (2.70) nm; IR (KBr) ν_{max} 1680, 1640 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.41 (t, J = 7.5 Hz, 3H), 3.38 (s, 3H), 3.44 (s, 3H), 3.75 (s, 3H), 4.48 (q, J = 7.5 Hz, 4H), 5.04 (s, 2H), 7.04 (dd, J = 7.5 Hz, J = 1.5 Hz, 3H), 7.36 (t, J = 7.5 Hz, 2H); MS m/z 557 (M^+). Anal. Calcd for $C_{19}H_{23}N_3O_4$: C, 63.86; H, 6.44; N, 11.76. Found: C, 63.90; H, 6.55; N, 11.66.

1,3-Dimethyl-5-ethyl-7-(methoxymethyl)-6-[(4′-methoxyphenoxy)methyl]pyrrolo[3,2-*d*]pyrimidine-2,4-dione (11d): yield 93%; mp 168 °C; λ_{max} (log ϵ) 224 (3.11), 272 (2.79) nm; IR (KBr) ν_{max} 1680, 1640 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.40 (t, J = 7.5 Hz, 3H), 3.37 (s, 3H), 3.43 (s, 3H), 3.73 (s, 3H), 3.79 (s, 3H), 4.47 (q, J = 7.5 Hz, 4H), 4.98 (s, 2H), 6.88−6.92 (m, 4H); MS m/z 387 (M^+). Anal. Calcd for $C_{20}H_{25}N_3O_5$: C, 62.01; H, 6.45; N, 10.85. Found: C, 62.11; H, 6.55; N, 10.93.

1,3-Dimethyl-5-ethyl-7-(methoxymethyl)-6-[(4′-methylphenoxy)methyl]pyrrolo[3,2-*d*]pyrimidine-2,4-dione (11e): yield 95%; mp 140 °C; λ_{max} (log ϵ) 225 (3.05), 275 (2.76) nm; IR (KBr) ν_{max} 1685, 1645 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.41 (t, J = 10.5 Hz, 3H), 2.33 (s, 3H), 3.35 (s, 3H),3.42 (s, 3H), 3.73 (s, 3H), 4.47 (q, J = 7.5 Hz, 4H), 4.98 (s, 2H), 6.84 (d, J = 2.5 Hz, 2H), 7.11 (d, J = 12 Hz, 2H); MS m/z 371 (M^+). Anal. Calcd for $C_{20}H_{25}N_3O_4$: C, 64.69; H, 6.73; N, 11.32. Found: C, 64.82; H, 6.81; N, 11.38.

1,3-Dimethyl-5-ethyl-7-(methoxymethyl)-6-[(2′-methylphenoxy)methyl]pyrrolo[3,2-*d*]pyrimidine-2,4-dione (11f): yield 95%; mp 148 °C; λ_{max} (log ϵ) 224 (3.50), 272 (3.20) nm; IR (KBr) ν_{max}; 1685, 1640 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.41 (t, J = 10.5 Hz, 3H), 2.16 (s, 3H), 3.34 (s, 3H), 3.42 (s, 3H), 3.73 (s, 3H), 4.49 (q, J = 10.5 Hz, 4H), 5.01 (s, 2H), 6.94 (d, J = 9 Hz, 2H), 7.16 (d, J = 12 Hz, 2H); MS m/z 371 (M^+). Anal. Calcd for $C_{20}H_{25}N_3O_4$: C, 64.69; H, 6.73; N, 11.32. Found: C, 64.71; H, 6.77; N, 11.45.

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