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A Novel Synthesis of Pyrano[2,3-*d*]pyrimidine Derivatives

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Abstract: A ready one-pot preparation for pyrano[2,3-*d*]pyrimidines from appropriately substituted pyran derivative and *N,N*-dimethyldichloromethyleniminium chloride (phosgeniminium chloride) is reported.

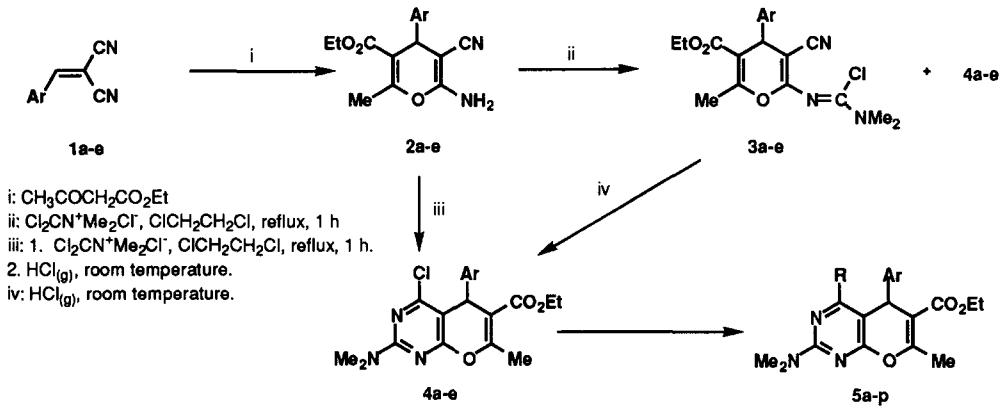
There is a continuous widespread interest in the synthesis of pyranopyrimidines because of the diverse physiological activities[1] associated with this system. Although a number of methods for the preparation of these compounds have been developed, most of them are based on barbituric or thiobarbituric acids and their alkylidene or arylidene derivatives as starting materials and usually several steps were needed.[2] Other synthesis start from amidoxime ethers which are cyclized with malonyl chloride or malonic acid in the presence of acetic anhydride[3] and by treatment of 6-hydroxipyrimidin-4-ones with bis-2,4,6-trichlorophenyl or diethyl malonates.[4] Also, condensation of substituted 6-aminopyrimidines with malonic acid derivatives affords pyrano[2,3-*d*]pyrimidines[5] and, in a paper recently published,[6] phosphorylated 2-amino-4*H*-pyran-3-carboxylates have been used in the synthesis of 4*H*-pyrano[2,3-*d*]pyrimidines by treatment with phenyl isocyanate.

Phosgeniminium chlorides are valuable strong electrophilic one carbon atom reagents. They possess three very mobile chlorine atoms and condense readily with nucleophiles to give new electrophilic synthons such as amide chlorides, α–chloroenamines, 1-3-dichlorotrimethinecyanines, etc, which react further to produce, through either inter or intramolecular processes, various types of functionalized 5, 6 and 7 membered ring systems.[7] Recently, some new methods for the preparation of polyheterocyclic compounds containing the pyrimidine ring utilizing phosgeniminium chloride have been developed in our laboratory.[8]

In search of an efficient method for the preparation of pyranopyrimidine compounds and following our work on the synthesis, reactivity and biological activity of polyheterocyclic systems which contain a pyrimidine moiety,[9] this paper describes a novel and convenient synthesis of some new pyrano[2,3-*d*]pyrimidines involving 2-amino-3-cyano-4*H*-pyran derivatives and *N,N*-dimethyldichloromethyleniminium chloride as starting materials.

The ethyl 2-amino-4-aryl-3-cyano-6-methyl-4*H*-pyran-5-carboxylates **2a-e**, used in this study, were prepared *via* refluxing arylidenemalononitriles **1a-e** with ethyl acetoacetate by a previously reported method.[10] On treatment with (dichloromethylene)-dimethylammonium chloride in refluxing 1,2-dichloroethane the pyran derivatives **2** afforded a mixture of the amide halide intermediates **3** and the pyranopyrimidines **4** which were isolated by concentration of the reaction mixture and purified by medium-pressure chromatography. Intermediates **3** underwent cyclization to the corresponding fused heterocyclic compounds **4** *via* reaction with dry hydrogen chloride.

Scheme 1



1-4	Ar	5	Ar	R	5	Ar	R
a	C_6H_5	a	C_6H_5	Piperidino	i	4-$OCH_3C_6H_4$	Morpholino
b	2-$OCH_3C_6H_4$	b	C_6H_5	Morpholino	j	4-$OCH_3C_6H_4$	4-Benzylpiperazino
c	4-$OCH_3C_6H_4$	c	C_6H_5	4-Benzylpiperazino	k	4-ClC_6H_4	Piperidino
d	4-ClC_6H_4	d	C_6H_5	4-Methylpiperazino	l	4-ClC_6H_4	Morpholino
e	3,4-$CH_2O_2C_6H_3$	e	2-$OCH_3C_6H_4$	Piperidino	m	4-ClC_6H_4	4-Benzylpiperazino
		f	2-$OCH_3C_6H_4$	Morpholino	n	3,4-$CH_2O_2C_6H_3$	Piperidino
		g	2-$OCH_3C_6H_4$	4-Benzylpiperazino	o	3,4-$CH_2O_2C_6H_3$	Morpholino
		h	4-$OCH_3C_6H_4$	Piperidino	p	3,4-$CH_2O_2C_6H_3$	4-Benzylpiperazino

One-pot synthesis using **2** and phosgeniminium salt in refluxing 1,2-dichloroethane for 1 hour and subsequent treatment with hydrogen chloride provided the substituted pyranopyrimidines **4a-e** in 80-90% yields. The structure of compounds **3** and **4** were consistent with their elemental analyses and spectral data. The mass spectra showed the expected molecular ion peak and the IR spectra of **3** exhibited an absorption band at $\nu = 1630$ cm^{-1} due to the imino group and presented a characteristic signal at $\nu = 2220$ cm^{-1}, while the decoupled ^{13}C NMR spectra showed one signal at $\delta = 118.0$-118.2 due to the carbon atom in the one cyano

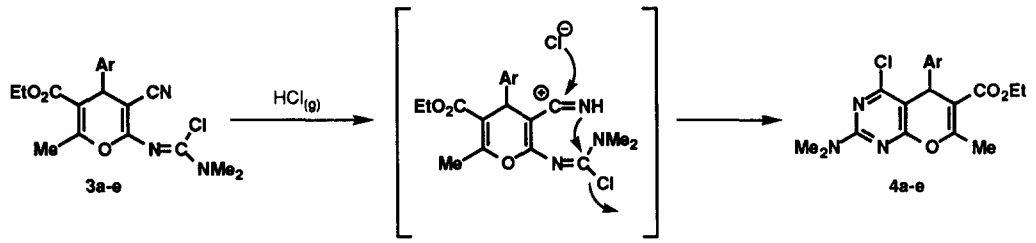
group. Nevertheless, spectra of compounds **4a-e** did not include those types of signals. The most salient features of the ^{1}H NMR and ^{13}C NMR spectra are summarized under Experimental.

Since the intermediate adducts **3** were isolated the reaction can be assumed to proceed as outlined in Scheme 2.[11]

Nucleophilic displacement reaction of the chloride bearing group in the bicyclic compounds **4** resulted in the formation on the corresponding substituted products **5** in good yields. Compounds **5** were characterized from microanalytical and spectral data.

This synthetic approach may be useful in view of the pharmacological interest in this compound class and shows that the reaction of *o*-aminocyanopyrans with (dichloromethylene)-dimethylammonium chloride provides a new, general route to pyrano[2,3-*d*]pyrimidines bearing various substituents at position 4 of the pyrimidine ring. Even though, there are many available methods for synthesizing pyranopyrimidines, to our knowledge, this is the first example of annelation of a pyrimidine ring to an existing pyran system using phosgeniminium chloride. In its simplicity, the affordability of the starting materials, good yields obtained and straightforward product isolation, the proposed one-pot procedure compares favourably with other syntheses for the pyrano[2,3-*d*]pyrimidine ring system.

Scheme 2



EXPERIMENTAL SECTION

All reagents used were commercial grade chemicals from freshly opened containers. Melting points were determined on a Büchi 510 apparatus and are reported uncorrected. IR spectra were recorded on potassium bromide disks on a Perkin-Elmer 383 spectrophotometer. ^{1}H and ^{13}C NMR spectra were obtained on a Bruker AC200F instrument at room temperature. Mass spectra were obtained on a VG4 spectrometer. The Silica gel 60 $HF_{254+366}$ used for analytical thin layer chromatography and the Silica gel 60 (230-400 mesh) employed for medium-pressure chromatography were purchased from Merck. Microanalyses for C, H, and N were performed by the Elemental Analyses General Service of the University of La Coruña.

Ethyl 2-amino-4-aryl-3-cyano-6-methyl-4H-pyran-5-carboxylates 2a-e:

Compounds **2a** and **2b** were prepared and isolated according to the reported procedure.[10] Pyran derivatives **2c-e** were obtained in a similar preparation from the appropriately arylidenemalonotrile and ethyl acetoacetate.

Ethyl 2-amino-3-cyano-4-(4-methoxyphenyl)-6-methyl-4H-pyran-5-carboxylate **2c** (50 %). Recrystallized from EtOH; mp 137-139 °C. IR (KBr): 3400, 3320 (NH); 2220 (CN); 1700 (CO). ^{1}H NMR δ ($CDCl_3$): 1.11 (t, 3H, J = 7.1 Hz, CH_2CH_3); 2.33 (d, 3H, J = 0.8 Hz, CH_3); 3.76 (s, 3H, OCH_3); 4.05 (q, 2H, J = 7.1 Hz, CH_2O); 4.39 (s, 1H, H-4); 4.62 (s, 2H, NH_2); 6.81, 7.11 (AA'BB' system, 4H, J = 8.7 Hz, $C_6H_4OCH_3$). ^{13}C NMR δ ($CDCl_3$): 13.8 (CH_2CH_3); 18.3 (CH_3); 37.9 (C-4); 55.1 (OCH_3); 60.5 (CH_2O); 62.0 (C-3); 108.1 (C-5); 113.8 (C-3'); 119.1 (CN); 128.5 (C-2'), 136.5 (C-1'); 156.6 (C-4'); 157.4, 158.5 (C-2, C-6); 166.0 (CO). MS (DEI): 314 (M^+, 46); 307 (100). Anal. Calcd. for $C_{17}H_{18}N_2O_4$: C, 64.96; H, 5.77; N, 8.91. Found C, 65.11; H, 5.53; N, 9.06.

Ethyl 2-amino-4-(4-chlorophenyl)-3-cyano-6-methyl-4H-pyran-5-carboxylate **2d** (71 %). Recrystallized from EtOH; mp 175-177 °C. IR (KBr): 3400, 3320 (NH); 2220 (CN); 1710 (CO). ^{1}H NMR δ ($CDCl_3$): 1.10 (t, 3H, J = 7.1 Hz, CH_2CH_3); 2.35 (d, 3H, J = 0.8 Hz, CH_3); 4.03 (q, 2H, J = 7.1 Hz, CH_2O); 4.41 (d, 1H, J = 0.7 Hz, H-4); 4.70 (s, 2H, NH_2); 7.13, 7.26 (AA'BB' system, 4H, J = 8.5 Hz, C_6H_4Cl). ^{13}C NMR δ ($CDCl_3$): 13.8 (CH_2CH_3); 18.4 (CH_3); 38.2 (C-4); 60.7 (CH_2O); 61.5 (C-3); 107.4 (C-5); 118.8 (CN); 128.6, 128.8, 132.8, 142.4 (C_6H_4Cl); 157.0, 157.6 (C-2, C-6); 165.6 (CO). MS (DEI): 320 (M^++2, 2); 318 (M^+, 6). Anal. Calcd. for $C_{16}H_{15}N_2O_3Cl$: C, 60.29; H, 4.74; N, 8.79. Found C, 60.10; H, 4.79; N, 8.61.

Ethyl 2-amino-3-cyano-6-methyl-4-(3,4-methylendioxyphenyl)-4H-pyran-5-carboxylate **2e** (62 %). Recrystallized from EtOH; mp 158-160 °C. IR (KBr): 3400, 3330 (NH); 2220 (CN); 1700 (CO). ^{1}H NMR δ ($CDCl_3$): 1.13 (t, 3H, J = 7.1 Hz, CH_2CH_3); 2.33 (d, 3H, J = 0.8 Hz, CH_3); 4.05 (q, 2H, J = 7.1 Hz, CH_2O); 4.35 (d, 1H, J = 0.8 Hz, H-4); 4.62 (s, 2H, NH_2); 5.91 (s, 3H, OCH_2O); 6.64-6.73 (m, 3H, $C_6H_3O_2CH_2$). ^{13}C NMR δ ($CDCl_3$): 13.9 (CH_2CH_3); 18.3 (CH_3); 38.4 (C-4); 60.6 (CH_2O); 61.9 (C-3); 100.9 (OCH_2O); 107.8, 108.0 (C-2', C-5'); 119.0 (CN); 120.8 (C-6'), 137.8 (C-1'); 146.5; 147.7; 156.4, 157.5 (C-2, C-6); 165.8 (CO). MS (DEI): 328 (M^+, 60); 207 (100). Anal. Calcd. for $C_{17}H_{16}N_2O_5$: C, 62.19; H, 4.91; N, 8.53. Found C, 62.07; H, 4.77; N, 8.68.

Ethyl 4-aryl-2-chlorodimethylaminomethylenamino-3-cyano-6-methyl-4H-pyran-5-carboxylates 3a-e; General Procedure.

A solution of **2** (3.5 mmol) and phosgeneiminium salt (4.2 mmol) in 1,2-dichloroethane (30 ml) was refluxed for 1 h. The solvent was removed under reduced pressure and the resulting solid was purified by MPLC using hexane/ethyl acetate (6:1) as eluent to obtain **3** and **4**.

Ethyl 2-chlorodimethylaminomethylenamino-3-cyano-6-methyl-4-phenyl-4H-pyran-5-carboxylate **3a** (89 %), (10 % **4a**); mp 110-112 °C. IR (KBr): 2220 (CN); 1710 (CO); 1630. ^{1}H NMR δ ($CDCl_3$): 1.11 (t, 3H, J = 7.2 Hz, CH_2CH_3); 2.39 (s, 3H, CH_3); 3.19 (s, 6H, NMe_2); 4.03 (q, 2H, J = 7.2 Hz, CH_2O); 4.54 (s, 1H, H-4); 7.21-7.31 (m, 5H, C_6H_5). ^{13}C NMR δ ($CDCl_3$): 13.7 (CH_2CH_3); 18.4 (CH_3); 40.2 (NMe_2); 40.5 (C-4); 60.2 (CH_2O); 78.2 (C-3); 106.3 (C-5); 118.0 (CN); 127.0, 127.7, 128.2, 143.1 (C_6H_5); 143.7 (C=N); 157.6, 158.1 (C-2, C-6); 165.8 (CO). MS (DEI): 375 (M^++2, 11); 373 (M^+, 31); 344 (15); 296 (100); 198 (22). Anal. Calcd. for $C_{19}H_{20}N_3O_3Cl$: C, 61.04; H, 5.39; N, 11.24. Found C, 61.18; H, 5.47; N, 11.12.

Ethyl 2-chlorodimethylaminomethylenamino-3-cyano-6-methyl-4-(2-methoxyphenyl)-4H-pyran-5-carboxylate **3b** (42 %), (58 % **4b**); mp 117-119 °C. IR (KBr): 2220 (CN); 1710 (CO); 1630. ^{1}H NMR δ ($CDCl_3$): 1.06

(t, 3H, J = 7.1 Hz, CH_2CH_3); 2.39 (s, 3H, CH_3); 3.17 (s, 6H, NMe_2); 3.84 (s, 3H, OCH_3); 4.01 (q, 2H, J = 7.1 Hz, CH_2O); 5.02 (s, 1H, H-4); 6.84-7.18 (m, 4H, $C_6H_4OCH_3$). ^{13}C NMR δ ($CDCl_3$): 13.6 (CH_2CH_3); 18.4 (CH_3); 34.0 (C-4); 40.2 (NMe_2); 55.4 (OCH_3); 60.1 (CH_2O); 77.7 (C-3); 105.5 (C-5); 110.6; 118.2 (CN); 120.4; 128.2; 129.2; 131.3; 143.6 (C=N); 156.8; 157.9, 158.8 (C-2, C-6); 166.1 (CO). MS (DEI): 405 (M^++2, 4); 403 (M^+, 10); 374 (44); 368 (92); 296 (48). Anal. Calcd. for $C_{20}H_{22}N_3O_4Cl$: C, 59.48; H, 5.49; N, 10.41. Found C, 59.64; H, 5.57; N, 10.35.

Ethyl 2-chlorodimethylaminomethylenamino-3-cyano-6-methyl-4-(4-methoxyphenyl)-4H-pyran-5-carboxylate ***3c*** (21 %), (66 % ***4c***); mp 126-128 °C. IR (KBr): 2220 (CN); 1710 (CO); 1630. ^1H NMR δ ($CDCl_3$): 1.13 (t, 3H, J = 7.1 Hz, CH_2CH_3); 2.36 (s, 3H, CH_3); 3.17 (s, 6H, NMe_2); 3.76 (s, 3H, OCH_3); 4.03 (q, 2H, J = 7.1 Hz, CH_2O); 4.49 (s, 1H, H-4); 6.82, 7.18 (AA'BB' sytem, 4H, J = 8.7 Hz, $C_6H_4OCH_3$). ^{13}C NMR δ ($CDCl_3$): 13.8 (CH_2CH_3); 18.5 (CH_3); 39.8 (C-4); 40.3 (NMe_2); 55.1 (OCH_3); 60.4 (CH_2O); 78.6 (C-3); 106.7 (C-5); 113.7; 118.2 (CN); 128.9; 135.6; 143.8 (C=N); 157.5; 157.8, 158.6 (C-2, C-6); 166.0 (CO). MS (DEI): 405 (M^++2, 16); 403 (M^+, 47); 374 (25); 368 (10); 296 (100). Anal. Calcd. for $C_{20}H_{22}N_3O_4Cl$: C, 59.48; H, 5.49; N, 10.41. Found C, 59.64; H, 5.57; N, 10.35.

Ethyl 2-chlorodimethylaminomethylenamino-4-(4-chlorophenyl)-3-cyano-6-methyl-4H-pyran-5-carboxylate ***3d*** (58 %), (32 % ***4d***); mp 132-134 °C. IR (KBr): 2210 (CN); 1720 (CO); 1630. ^1H NMR δ ($CDCl_3$): 1.12 (t, 3H, J = 7.1 Hz, CH_2CH_3); 2.38 (d, 3H, J = 0.8 Hz, CH_3); 3.19 (s, 6H, NMe_2); 4.04 (q, 2H, J = 7.1 Hz, CH_2O); 4.52 (d, 1H, J = 0.7 Hz, H-4); 7.20, 7.27 (AA'BB' system, 4H, J = 8.6 Hz, C_6H_4Cl). ^{13}C NMR δ ($CDCl_3$): 13.9 (CH_2CH_3); 18.6 (CH_3); 40.2 (C-4); 40.4 (NMe_2); 60.5 (CH_2O); 78.0 (C-3); 106.1 (C-5); 118.0 (CN); 128.6, 129.2, 133.0, 141.9 (C_6H_4Cl); 144.0 (C=N); 157.8, 158.6 (C-2, C-6); 165.8 (CO). MS (DEI): 409 (M^++2, 21); 407 (M^+, 32); 378 (20); 296 (100). Anal. Calcd. for $C_{19}H_{19}N_3O_3Cl_2$: C, 55.90; H, 4.69; N, 10.29. Found C, 56.10; H, 4.49; N, 10.21.

Ethyl 2-chlorodimethylaminomethylenamino-3-cyano-6-methyl-4-(3,4-methylendioxyphenyl)-4H-pyran-5-carboxylate ***3e*** (79 %), (5% ***4e***); mp 102-103 °C. IR (KBr): 2220 (CN); 1700 (CO); 1630. ^1H NMR δ ($CDCl_3$): 1.16 (t, 3H, J = 7.1 Hz, CH_2CH_3); 2.36 (d, 3H, J = 0.8 Hz, CH_3); 3.19 (s, 6H, NMe_2); 4.06 (q, 2H, J = 7.1 Hz, CH_2O); 4.46 (d, 1H, J = 0.8 Hz, H-4); 5.92 (s, 3H, OCH_2O); 6.73-6.76 (m, 3H, $C_6H_3CH_2O_2$). ^{13}C NMR δ ($CDCl_3$): 13.9 (CH_2CH_3); 18.5 (CH_3); 40.3 (C-4); 40.4 (NMe_2); 60.5 (CH_2O); 78.5 (C-3); 100.9 (OCH_2O); 106.5 (C-5); 108.0, 108.2 (C-2', C-5'); 118.1 (CN); 121.2 (C-6'), 137.4 (C-1'); 143.9 (C=N); 146.6; 147.7; 156.6, 157.9 (C-2, C-6); 165.9 (CO). MS (DEI): 419 (M^++2, 18); 417 (M^+, 49); 388 (22); 312 (22); 296 (100). Anal. Calcd. for $C_{20}H_{20}N_3O_5Cl$: C, 57.49; H, 4.82; N, 10.06. Found C, 57.27; H, 4.95; N, 10.18.

Ethyl 5-aryl-4-chloro-2-dimethylamino-7-methyl-5H-pyrano[2,3-d]pyrimidin-6-carboxylates 4a-e; General Procedure.

Method A:

A solution of **2** (3.5 mmol) and phosgeneiminium salt (4.2 mmol) in 1,2-dichloroethane (30 ml) was refluxed for 1 h. A stream of dry hydrogen chloride was passed through a mixture for 3 h and the reaction

mixture was allowed to stand overnight at room temperature. The solvent was then removed under reduced pressure and the resulting solid was recrystallized from EtOH to obtain **4**.

Ethyl 4-chloro-2-dimethylamino-7-methyl-5-phenyl-5H-pyrano[2,3-d]pyrimidin-6-carboxylate ***4a*** (95 %); mp 120-122 °C. IR (KBr): 1720 (CO). ^{1}H NMR δ ($CDCl_3$): 1.24 (t, 3H, J = 7.1 Hz, CH_2CH_3); 2.50 (s, 3H, CH_3); 3.14 (s, 6H, NMe_2); 4.13 (q, 2H, J = 7.1 Hz, CH_2O); 4.97 (s, 1H, H-5); 7.15-7.24 (m, 5H, C_6H_5). ^{13}C NMR δ ($CDCl_3$): 14.0 (CH_2CH_3); 19.1 (CH_3); 37.1 (NMe_2); 38.8 (C-5); 60.0 (CH_2O); 101.9 (C-4a); 109.5 (C-6); 126.8, 128.1, 128.6, 143.6 (C_6H_5); 158.6, 159.9, 160.8, 163.3 (C-2, C-4, C-7, C-8a); 166.0 (CO). MS (DEI): 375 (M^++2, 5); 373 (M^+, 15); 344 (7); 296 (100); 268 (19). Anal. Calcd. for $C_{19}H_{20}N_3O_3Cl$: C, 61.04; H, 5.39; N, 11.24. Found C, 60.89; H, 5.21; N, 11.17.

Ethyl 4-chloro-2-dimethylamino-5-(2-methoxyphenyl)-7-methyl-5H-pyrano[2,3-d]pyrimidin-6-carboxylate ***4b*** (87 %); mp 178-180 °C. IR (KBr): 1710 (CO). ^{1}H NMR δ ($CDCl_3$): 1.23 (t, 3H, J = 7.1 Hz, CH_2CH_3); 2.46 (s, 3H, CH_3); 3.13 (s, 6H, NMe_2); 3.70 (s, 3H, OCH_3); 4.08 (q, 2H, J = 7.1 Hz, CH_2O); 5.04 (s, 1H, H-5); 6.75-7.32 (m, 4H, $C_6H_4OCH_3$). ^{13}C NMR δ ($CDCl_3$): 13.9 (CH_2CH_3); 18.9 (CH_3); 36.3 (C-5); 37.1 (NMe_2); 55.0 (OCH_3); 60.3 (CH_2O); 101.0 (C-4a); 106.5 (C-6); 111.2, 119.6, 128.2, 129.8, 132.2, 157.7 ($C_6H_4OCH_3$); 158.9; 159.8; 164.0; 166.3 (CO). MS (DEI): 405 (M^++2, 5); 403 (M^+, 12); 374 (11); 326 (48); 296 (62). Anal. Calcd. for $C_{20}H_{22}N_3O_4Cl$: C, 59.48; H, 5.49; N, 10.41. Found C, 59.55; H, 5.31; N, 10.47.

Ethyl 4-chloro-2-dimethylamino-5-(4-methoxyphenyl)-7-methyl-5H-pyrano[2,3-d]pyrimidin-6-carboxylate ***4c*** (80 %); mp 140-141 °C. IR (KBr): 1710 (CO). ^{1}H NMR δ ($CDCl_3$): 1.25 (t, 3H, J = 7.1 Hz, CH_2CH_3); 2.49 (s, 3H, CH_3); 3.14 (s, 6H, NMe_2); 3.75 (s, 3H, OCH_3); 4.13 (q, 2H, J = 7.1 Hz, CH_2O); 4.91 (s, 1H, H-5); 6.76, 7.19 (AA'BB' system, 4H, J = 8.7 Hz, $C_6H_4OCH_3$). ^{13}C NMR δ ($CDCl_3$): 14.1 (CH_2CH_3); 19.0 (CH_3); 37.1 (NMe_2); 37.9 (C-5); 55.1 (OCH_3); 60.6 (CH_2O); 102.1 (C-4a); 109.7 (C-6); 113.4, 129.6, 135.9, 158.2 ($C_6H_4OCH_3$); 159.8; 160.8; 163.3; 166.0 (CO). MS (DEI): 405 (M^++2, 8); 403 (M^+, 23); 374 (15); 330 (44); 296 (100). Anal. Calcd. for $C_{20}H_{22}N_3O_4Cl$: C, 59.48; H, 5.49; N, 10.41. Found C, 59.37; H, 5.27; N, 10.63.

Ethyl 4-chloro-5-(4-chlorophenyl)-2-dimethylamino-7-methyl-5H-pyrano[2,3-d]pyrimidin-6-carboxylate ***4d*** (83 %); mp 152-154 °C. IR (KBr): 1710 (CO). ^{1}H NMR δ ($CDCl_3$): 1.25 (t, 3H, J = 7.1 Hz, CH_2CH_3); 2.50 (s, 3H, CH_3); 3.15 (s, 6H, NMe_2); 4.13 (q, 2H, J = 7.1 Hz, CH_2O); 4.94 (s, 1H, H-5); 7.14-7.25 (m, 4H, C_6H_4Cl). ^{13}C NMR δ ($CDCl_3$): 14.0 (CH_2CH_3); 19.1 (CH_3); 37.1 (NMe_2); 38.2 (C-5); 60.7 (CH_2O); 101.3 (C-4a); 109.0 (C-6); 128.2, 128.9, 132.5, 142.1 (C_6H_4Cl); 158.8, 159.9, 160.8; 163.2 (C-2, C-4, C-7, C-8a); 165.7 (CO). MS (DEI): 411 (M^++4, 3); 409 (M^++2, 14); 407 (M^+, 22); 378 (14); 296 (100). Anal. Calcd. for $C_{19}H_{19}N_3O_3Cl_2$: C, 55.90; H, 4.69; N, 10.29. Found C, 55.81; H, 4.54; N, 10.43.

Ethyl 4-chloro-2-dimethylamino-7-methyl-5-(3,4-methylendioxyphenyl)-5H-pyrano[2,3-d]pyrimidin-6-carboxylate ***4e*** (90 %); mp 156-158 °C. IR (KBr): 1710 (CO). ^{1}H NMR δ ($CDCl_3$): 1.25 (t, 3H, J = 7.1 Hz, CH_2CH_3); 2.48 (d, 3H, J = 0.7 Hz, CH_3); 3.14 (s, 6H, NMe_2); 4.15 (q, 2H, J = 7.1 Hz, CH_2O); 4.89 (s, 1H, J = 0.7 Hz, H-5); 5.89 (s, 2H, OCH_2O); 6.64-6.75 (m, 3H, C_6H_3). ^{13}C NMR δ ($CDCl_3$): 14.1 (CH_2CH_3); 19.0 (CH_3); 37.1 (NMe_2); 38.4 (C-5); 60.6 (CH_2O); 100.9 (OCH_2O); 101.8 (C-4a); 109.5 (C-6);

107.7, 108.9, 121.9, 137.6, 146.2, 147.3 (C_6H_3); 158.3, 159.8, 160.7; 163.2 (C-2, C-4, C-7, C-8a); 166.0 (CO). MS (DEI): 419 (M^++2, 10); 417 (M^+, 25); 388 (10); 371 (10); 344 (25); 296 (100). Anal. Calcd. for $C_{20}H_{20}N_3O_5Cl$: C, 57.49; H, 4.82; N, 10.06. Found C, 57.62; H, 4.98; N, 9.92.

Method B:

A stream of dry hydrogen chloride was passed through a mixture of **3** (3.0 mmol) in 1,2-dichloroethane (10 ml) for 3 h. The reaction mixture was allowed to stand overnight at room temperature. The solvent was then removed under reduced pressure and the resulting solid was recrystallized from EtOH to obtain **4a** (85 %), **4b** (70 %), **4c** (70 %), **4d** (75 %), **4e** (60 %).

Ethyl 2-dimethylamino-7-methyl-5-phenyl-5H-pyrano[2,3-d]pyrimidin-6-carboxylate 4-substituted; 5a-o. General Procedure.

A solution of **4** (0.3 mmol) and the appropriate amine (0.36 mmol) in EtOH (10 ml) was refluxed until all starting material had disappeared as checked by tlc (16-54 h). The solid obtained was then filtered off and recrystallized from EtOH.

Ethyl 2-dimethylamino-7-methyl-5-phenyl-4-piperidino-5H-pyrano[2,3-d]pyrimidin-6-carboxylate ***5a*** (62 %); mp 174-176 °C. IR (KBr): 1720 (CO). ^{1}H NMR δ ($CDCl_3$): 1.26 (t, 3H, J = 7.1 Hz, CH_2CH_3); 1.59-1.73 (m, 6H), 2.47 (s, 3H, CH_3); 3.11-3.37 (m, 10H, NCH_2, NMe_2); 4.16 (q, 2H, J = 7.1 Hz, CH_2O); 4.99 (s, 1H, H-5); 7.08-7.26 (m, 5H, C_6H_5). ^{13}C NMR δ ($CDCl_3$): 14.1 (CH_2CH_3); 19.4 (CH_3); 24.6, 25.7 (CH_2); 36.8 (NMe_2); 37.6 (C-5); 50.1 (NCH_2); 60.4 (CH_2O); 91.2 (C-4a); 109.2 (C-6); 126.3, 127.5, 128.0, 145.1 (C_6H_5); 159.6; 160.0; 164.5; 166.7 (CO). MS (DEI): 422 (M^+, 40); 379 (18); 345 (100); 317 (15). Anal. Calcd. for $C_{24}H_{30}N_4O_3$: C, 68.22; H, 7.16; N, 13.26. Found C, 68.41; H, 7.10; N, 13.52.

Ethyl 2-dimethylamino-7-methyl-4-morpholino-5-phenyl-5H-pyrano[2,3-d]pyrimidin-6-carboxylate ***5b*** (66 %); mp 142-144 °C. IR (KBr): 1710 (CO). ^{1}H NMR δ ($CDCl_3$): 1.25 (t, 3H, J = 7.1 Hz, CH_2CH_3); 2.45 (s, 3H, CH_3); 3.11 (s, 6H, NMe_2); 3.13-3.20 (m, 2H, NCH_2); 3.34-3.45 (m, 2H, NCH_2); 3.60-3.79 (m, 4H, OCH_2); 4.15 (q, 2H, J = 7.1 Hz, CH_2O); 4.96 (s, 1H, H-5); 7.11-7.27 (m, 5H, C_6H_5). ^{13}C NMR δ ($CDCl_3$): 14.1 (CH_2CH_3); 19.3 (CH_3); 36.7 (NMe_2); 37.5 (C-5); 49.1 (NCH_2); 60.4 (CH_2O); 66.5 (OCH_2); 91.5 (C-4a); 109.0 (C-6); 126.5, 127.5, 128.0, 144.6 (C_6H_5); 159.0, 160.0, 164.5, 166.0 (C-2, C-4, C-7, C-8a); 166.5 (CO). MS (DEI): 424 (M^+, 29); 379 (8); 347 (100); 319 (15). Anal. Calcd. for $C_{23}H_{28}N_4O_4$: C, 65.08; H, 6.65; N, 13.20. Found C, 64.93; H, 6.77; N, 13.03.

Ethyl 4-(4-benzylpiperazino)-2-dimethylamino-7-methyl-5-phenyl-5H-pyrano[2,3-d]pyrimidin-6-carboxylate ***5c*** (51 %); mp 190-192 °C. IR (KBr): 1710 (CO). ^{1}H NMR δ ($CDCl_3$): 1.25 (t, 3H, J = 7.1 Hz, CH_2CH_3); 2.38-2.59 (m, 4H, NCH_2); 2.46 (s, 3H, CH_3); 3.14-3.50 (m, 4H, NCH_2); 3.10 (s, 6H, NMe_2); 3.53 (s, 2H, NCH_2); 4.15 (q, 2H, J = 7.1 Hz, CH_2O); 4.97 (s, 1H, H-5); 7.09-7.35 (m, 10H, C_6H_5). ^{13}C NMR δ ($CDCl_3$): 14.1 (CH_2CH_3); 19.4 (CH_3); 36.8 (NMe_2); 37.5 (C-5); 48.7 (NCH_2); 52.8 (NCH_2); 60.4 (CH_2O); 63.0 (NCH_2Ph); 91.3 (C-4a); 109.1 (C-6); 126.4, 127.0, 127.6; 128.0, 128.2, 129.1, 137.9, 144.8 (C_6H_5); 159.3, 159.9, 164.6, 166.1 (C-2, C-4, C-7, C-8a); 166.7 (CO). MS (DEI): 513 (M^+, 19); 422 (49); 367 (88);

354 (19)339 (28). Anal. Calcd. for $C_{30}H_{35}N_5O_3$: C, 70.15; H, 6.87; N, 13.64. Found C, 70.01; H, 6.96; N, 13.47.

Ethyl 2-dimethylamino-7-methyl-4-(4-methylpiperazino)-5-phenyl-5H-pyrano[2,3-d]pyrimidin-6-carboxylate ***5d*** (83 %); mp 150-151 °C. IR (KBr): 1710 (CO). ^{1}H NMR δ ($CDCl_3$): 1.24 (t, 3H, J = 7.1 Hz, CH_2CH_3); 2.29 (s, 3H, NCH_3); 2.44 (s, 3H, CH_3); 2.33-2.54 (m, 4H, NCH_2); 3.10 (s, 6H, NMe_2); 3.08-3.26 (m, 2H, NCH_2); 3.36-3.48 (m, 2H, NCH_2); 4.14 (q, 2H, J = 7.1 Hz, CH_2O); 4.96 (s, 1H, H-5); 7.09-7.19 (m, 5H, C_6H_5). ^{13}C NMR δ ($CDCl_3$): 14.1 (CH_2CH_3); 19.4 (CH_3); 36.8 (NMe_2); 37.5 (C-5); 46.1 (NCH_3); 48.6 (NCH_2); 54.7 (NCH_2); 60.4 (CH_2O); 91.3 (C-4a); 109.1 (C-6); 126.4, 127.5, 128.0, 144.8 (C_6H_5); 159.3, 159.9, 164.5, 166.0 (C-2, C-4, C-7, C-8a); 166.6 (CO). MS (DEI): 437 (M^+, 37); 367 (100); 354 (29); 339 (34). Anal. Calcd. for $C_{24}H_{31}N_5O_3$: C, 65.88; H, 7.14; N, 16.01. Found C, 65.72; H, 7.06; N, 16.09.

Ethyl 2-dimethylamino-5-(2-methoxyphenyl)-7-methyl-4-piperidino-5H-pyrano[2,3-d]pyrimidin-6-carboxylate ***5e*** (79 %); mp 178-180 °C. IR (KBr): 1700 (CO). ^{1}H NMR δ ($CDCl_3$): 1.24 (t, 3H, J = 7.1 Hz, CH_2CH_3); 1.54-1.60 (m, 6H), 2.42 (s, 3H, CH_3); 3.10 (s, 6H, NMe_2); 3.12-3.29 (m, 4H, NCH_2); 3.74 (s, 3H, OCH_3); 4.11 (q, 2H, J = 7.1 Hz, CH_2O); 5.27 (s, 1H, H-5); 6.73-6.82 (m, 2H, $CH_3OC_6H_4$); 7.06-7.13 (m, 2H, $CH_3OC_6H_4$). ^{13}C NMR δ ($CDCl_3$): 14.1 (CH_2CH_3); 19.0 (CH_3); 24.6, 25.7 (CH_2); 33.1 (C-5); 36.8 (NMe_2); 50.2 (NCH_2); 55.1 (OCH_3); 60.1 (CH_2O); 90.7 (C-4a); 108.0 (C-6); 110.0, 120.0, 127.5, 130.1, 132.7, 156.8 ($CH_3OC_6H_4$); 158.6, 159.8, 165.1, 166.8 (C-2, C-4, C-7, C-8a); 167.2 (CO). MS (DEI): 452 (M^+, 45); 409 (22); 345 (100); 317 (17). Anal. Calcd. for $C_{25}H_{32}N_4O_4$: C, 66.35; H, 7.13; N, 12.38. Found C, 66.21; H, 7.00; N, 12.55.

Ethyl 2-dimethylamino-5-(2-methoxyphenyl)-7-methyl-4-morpholino-5H-pyrano[2,3-d]pyrimidin-6-carboxylate ***5f*** (46 %); mp 144-146 °C. IR (KBr): 1710 (CO). ^{1}H NMR δ ($CDCl_3$): 1.22 (t, 3H, J = 7.1 Hz, CH_2CH_3); 2.42 (s, 3H, CH_3); 3.09-3.12 (m, 2H); 3.10 (s, 6H, NMe_2); 3.64-3.67 (m, 2H); 3.74-3.78 (m, 4H); 3.76 (s, 3H, OCH_3); 4.11 (q, 2H, J = 7.1 Hz, CH_2O); 5.26 (s, 1H, H-5); 6.75-6.79 (m, 2H, $CH_3OC_6H_4$); 7.07-7.10 (m, 2H, $CH_3OC_6H_4$). ^{13}C NMR δ ($CDCl_3$): 14.0 (CH_2CH_3); 19.0 (CH_3); 32.5 (C-5); 36.8 (NMe_2); 49.4 (NCH_2); 55.2 (OCH_3); 60.2 (CH_2O); 66.6 (CH_2O); 91.3 (C-4a); 108.2 (C-6); 110.6, 120.2, 127.7, 130.1, 132.5, 156.5 ($CH_3OC_6H_4$); 158.3, 159.7, 165.1, 166.3 (C-2, C-4, C-7, C-8a); 166.9 (CO). MS (DEI): 454 (M^+, 37); 409 (12); 365 (17); 347 (100). Anal. Calcd. for $C_{24}H_{30}N_4O_5$: C, 63.42; H, 6.65; N, 12.33. Found C, 63.58; H, 6.49; N, 12.38.

Ethyl 4-(4-benzylpiperazino)-2-dimethylamino-5-(2-methoxyphenyl-7-methyl-5H-pyrano[2,3-d]pyrimidin-6-carboxylate ***5g*** (73 %); mp 206-208 °C. IR (KBr): 1710 (CO). ^{1}H NMR δ ($CDCl_3$): 1.22 (t, 3H, J = 7.1 Hz, CH_2CH_3); 2.35-2.60 (m, 4H, NCH_2); 2.41 (s, 3H, CH_3); 3.09 (s, 6H, NMe_2); 3.13-3.18 (m, 2H, NCH_2); 3.41-3.47 (m, 2H, NCH_2); 3.53 (s, 2H, NCH_2); 3.72 (s, 3H, OCH_3); 4.10 (q, 2H, J = 7.1 Hz, CH_2O); 5.25 (s, 1H, H-5); 6.73-6.81 (m, 2H, $CH_3OC_6H_4$); 7.05-7.13 (m, 2H, $CH_3OC_6H_4$); 7.26-7.34 (m, 10H, C_6H_5). ^{13}C NMR δ ($CDCl_3$): 14.1 (CH_2CH_3); 19.0 (CH_3); 32.8 (C-5); 36.8 (NMe_2); 48.8 (NCH_2); 52.8 (NCH_2); 55.1 (OCH_3); 60.2 (CH_2O); 63.1 (NCH_2Ph); 90.9 (C-4a); 108.0 (C-6); 110.6, 120.1, 127.0, 127.6; 128.1, 129.1, 130.2, 132.6, 137.9, 156.7 ($CH_3OC_6H_4$, C_6H_5); 158.5, 159.7, 165.1, 166.2 (C-2, C-4, C-7, C-8a); 167.1 (CO). MS (DEI): 543 (M^+, 12); 452 (33); 397 (67); 369 (12). Anal. Calcd. for $C_{31}H_{37}N_5O_4$: C, 68.49; H, 6.86; N, 12.88. Found C, 68.62; H, 6.71; N, 13.01.

Ethyl 2-dimethylamino-5-(4-methoxyphenyl)-7-methyl-4-piperidino-5H-pyrano[2,3-d]pyrimidin-6-carboxylate ***5h*** (63 %); mp 110-112 °C. IR (KBr): 1710 (CO). ^{1}H NMR δ ($CDCl_3$): 1.27 (t, 3H, J = 7.1 Hz, CH_2CH_3); 1.60-1.68 (m, 6H), 2.46 (s, 3H, CH_3); 3.12 (s, 6H, NMe_2); 3.14-3.32 (m, 4H, NCH_2); 3.74 (s, 3H, OCH_3); 4.16 (q, 2H, J = 7.1 Hz, CH_2O); 4.93 (s, 1H, H-5); 6.72, 7.18 (AA'BB' system, 4H, J = 8.7 Hz, $CH_3OC_6H_4$). ^{13}C NMR δ ($CDCl_3$): 14.2 (CH_2CH_3); 19.4 (CH_3); 24.6, 25.8 (CH_2); 30.9 (C-5); 36.8 (NMe_2); 50.1 (NCH_2); 55.1 (OCH_3); 60.4 (CH_2O); 91.5 (C-4a); 109.4 (C-6); 113.3, 128.5, 137.5, 158.0 ($CH_3OC_6H_4$); 159.3, 160.0, 164.5, 166.6 (C-2, C-4, C-7, C-8a); 166.8 (CO). MS (DEI): 452 (M^+, 50); 409 (23); 345 (100); 317 (16). Anal. Calcd. for $C_{25}H_{32}N_4O_4$: C, 66.35; H, 7.13; N, 12.38. Found C, 66.37; H, 7.03; N, 12.21.

Ethyl 2-dimethylamino-5-(4-methoxyphenyl)-7-methyl-4-morpholino-5H-pyrano[2,3-d]pyrimidin-6-carboxylate ***5i*** (50 %); mp 143-145 °C. IR (KBr): 1710 (CO). ^{1}H NMR δ ($CDCl_3$): 1.26 (t, 3H, J = 7.1 Hz, CH_2CH_3); 2.44 (s, 3H, CH_3); 3.12 (s, 6H, NMe_2); 3.14-3.22 (m, 2H); 3.34-3.45 (m, 2H); 3.61-3.79 (m, 4H); 3.74 (s, 3H, OCH_3); 4.16 (q, 2H, J = 7.1 Hz, CH_2O); 4.90 (s, 1H, H-5); 6.74, 7.15 (AA'BB' system, 4H, J = 8.7 Hz, $CH_3OC_6H_4$). ^{13}C NMR δ ($CDCl_3$): 14.2 (CH_2CH_3); 19.4 (CH_3); 36.7 (C-5); 36.8 (NMe_2); 49.2 (NCH_2); 55.1 (OCH_3); 60.5 (CH_2O); 66.6 (CH_2O); 91.7 (C-4a); 109.4 (C-6); 113.4, 128.6, 137.0, 158.1 ($CH_3OC_6H_4$); 159.0, 160.0, 164.6, 166.0 (C-2, C-4, C-7, C-8a); 166.7 (CO). MS (DEI): 454 (M^+, 48). Anal. Calcd. for $C_{24}H_{30}N_4O_5$: C, 63.42; H, 6.65; N, 12.33. Found C, 63.27; H, 6.77; N, 12.50.

Ethyl 4-(4-benzylpiperazino)-2-dimethylamino-5-(4-methoxyphenyl-7-methyl-5H-pyrano[2,3-d]pyrimidin-6-carboxylate ***5j*** (60 %); mp 166-168 °C. IR (KBr): 1710 (CO). ^{1}H NMR δ ($CDCl_3$): 1.24 (t, 3H, J = 7.1 Hz, CH_2CH_3); 2.44 (s, 3H, CH_3); 2.47-2.54 (m, 4H, NCH_2); 3.11 (s, 6H, NMe_2); 3.24-3.28 (m, 2H, NCH_2); 3.39-3.43 (m, 2H, NCH_2); 3.55 (s, 2H, NCH_2); 3.74 (s, 3H, OCH_3); 4.16 (q, 2H, J = 7.1 Hz, CH_2O); 4.91 (s, 1H, H-5); 6.71, 7.09 (AA'BB' system, 4H, J = 8.7 Hz, $CH_3OC_6H_4$); 7.29-7.35 (m, 10H, C_6H_5). ^{13}C NMR δ ($CDCl_3$): 14.2 (CH_2CH_3); 19.4 (CH_3); 31.0 (C-5); 36.8 (NMe_2); 48.6 (NCH_2); 52.9 (NCH_2); 55.1 (OCH_3); 60.5 (CH_2O); 63.0 (NCH_2Ph); 91.6 (C-4a); 109.4 (C-6); 113.4, 127.1, 128.2, 128.6, 129.2, 137.3, 137.8, 158.1 ($CH_3OC_6H_4$, C_6H_5); 159.1, 160.0, 164.6, 166.0 (C-2, C-4, C-7, C-8a); 166.8 (CO). MS (DEI): 543 (M^+, 3); 452 (13); 397 (19). Anal. Calcd. for $C_{31}H_{37}N_5O_4$: C, 68.49; H, 6.86; N, 12.88. Found C, 68.31; H, 6.97; N, 12.70.

Ethyl 5-(4-chlorophenyl)-2-dimethylamino-7-methyl-4-piperidino-5H-pyrano[2,3-d]pyrimidin-6-carboxylate ***5k*** (55 %); mp 166-168 °C. IR (KBr): 1700 (CO). ^{1}H NMR δ ($CDCl_3$): 1.26 (t, 3H, J = 7.1 Hz, CH_2CH_3); 1.59-1.67 (m, 6H), 2.47 (s, 3H, CH_3); 3.12 (s, 6H, NMe_2); 3.15-3.36 (m, 4H, NCH_2); 4.16 (q, 2H, J = 7.1 Hz, CH_2O); 4.95 (s, 1H, H-5); 7.10-7.19 (m, 4H, C_6H_4Cl). ^{13}C NMR δ ($CDCl_3$): 14.1 (CH_2CH_3); 19.4 (CH_3); 24.5, 25.7 (CH_2); 36.8 (NMe_2); 37.1 (C-5); 50.2 (NCH_2); 60.2 (CH_2O); 90.8 (C-4a); 108.7 (C-6); 128.1, 128.9, 132.0, 143.6 (C_6H_4Cl); 159.7, 160.1, 164.3; 166.6 (C-2, C-4, C-7, C-8a); 166.7 (CO). MS (DEI): 458 (M^++2, 11); 456 (M^+, 28); 413 (16); 345 (86); 317 (23). Anal. Calcd. for $C_{24}H_{29}N_4O_3Cl$; C, 63.08; H, 6.40; N, 12.26. Found C, 62.93; H, 6.91; N, 12.35.

Ethyl 5-(4-chlorophenyl)-2-dimethylamino-7-methyl-4-morpholino-5H-pyrano[2,3-d]pyrimidin-6-carboxylate ***5l*** (60 %); mp 190-191 °C. IR (KBr): 1710 (CO). ^{1}H NMR δ ($CDCl_3$): 1.25 (t, 3H, J = 7.1 Hz, CH_2CH_3);

2.45 (s, 3H, CH_3); 3.07-3.18 (m, 2H, NCH_2); 3.12 (s, 6H, NMe_2); 3.35-3.46 (m, 2H, NCH_2); 3.60-3.83 (m, 4H, OCH_2); 4.15 (q, 2H, J = 7.1 Hz, CH_2O); 4.92 (s, 1H, H-5); 7.09-7.19 (m, 4H, C_6H_4Cl). ^{13}C NMR δ ($CDCl_3$): 14.2 (CH_2CH_3); 19.5 (CH_3); 36.9 (NMe_2); 37.1 (C-5); 49.3 (NCH_2); 60.7 (CH_2O); 66.6 (OCH_2); 91.1 (C-4a); 108.7 (C-6); 128.3, 129.0, 132.2, 143.3 (C_6H_4Cl); 159.3, 160.0, 164.4, 166.2 (C-2, C-4, C-7, C-8a); 166.5 (CO). MS (DEI): 460 (M^++2, 8); 458 (M^+, 22); 347 (100). Anal. Calcd. for $C_{23}H_{27}N_4O_4Cl$: C, 60.19; H, 5.93; N, 12.21. Found C, 60.27; H, 5.81; N, 12.10.

Ethyl 4-(4-benzylpiperazino)-5-(4-chlorophenyl)-2-dimethylamino-7-methyl-5H-pyrano[2,3-d]pyrimidin-6-carboxylate ***5m*** (77 %); 192-194 °C. IR (KBr): 1710 (CO). ^1H NMR δ ($CDCl_3$): 1.25 (t, 3H, J = 7.1 Hz, CH_2CH_3); 2.38-2.60 (m, 4H, NCH_2); 2.46 (s, 3H, CH_3); 3.11 (s, 6H, NMe_2); 3.15-3.24 (m, 2H, NCH_2); 3.39-3.50 (m, 2H, NCH_2); 3.55 (s, 2H, NCH_2); 4.15 (q, 2H, J = 7.1 Hz, CH_2O); 4.93 (s, 1H, H-5); 7.08-7.18 (m, 4H, C_6H_4Cl); 7.24-7.36 (m, 5H, C_6H_5). ^{13}C NMR δ ($CDCl_3$): 14.2 (CH_2CH_3); 19.5 (CH_3); 36.8 (NMe_2); 37.1 (C-5); 48.7 (NCH_2); 52.8 (NCH_2); 60.6 (CH_2O); 63.0 (NCH_2Ph); 90.9 (C-4a); 108.7 (C-6); 127.2, 128.2, 128.3, 129.0, 129.2, 132.1, 137.6, 143.4 (C_6H_4Cl, C_6H_5); 159.5, 160.0, 164.4, 166.2 (C-2, C-4, C-7, C-8a); 166.5 (CO). MS (DEI): 549 (M^++2, 6); 547 (M^+, 15); 456 (30); 401 (55); 388 (16). Anal. Calcd. for $C_{30}H_{34}N_5O_3Cl$: C, 65.74; H, 6.25; N, 12.78. Found C, 65.90; H, 6.07; N, 12.91.

Ethyl 2-dimethylamino-7-methyl-5-(3,4-methylendioxyphenyl)-4-piperidino-5H-pyrano[2,3-d]pyrimidin-6-carboxylate ***5n*** (86 %); mp 137-139 °C. IR (KBr): 1710 (CO). ^1H NMR δ ($CDCl_3$): 1.27 (t, 3H, J = 7.1 Hz, CH_2CH_3); 1.60-1.68 (m, 6H); 2.45 (s, 3H, CH_3); 3.11 (s, 6H, NMe_2); 3.14-3.35 (m, 4H); 4.17 (q, 2H, J = 7.1 Hz, CH_2O); 4.92 (s, 1H, H-5); 5.86 (s, 2H, OCH_2O); 6.63-6.69 (m, 3H, C_6H_3). ^{13}C NMR δ ($CDCl_3$): 14.1 (CH_2CH_3); 19.4 (CH_3); 24.6, 25.7 (CH_2); 36.8 (NMe_2); 37.2 (C-5); 50.1 (NCH_2); 60.4 (CH_2O); 91.1 (C-4a); 100.7 (OCH_2O); 109.2 (C-6); 107.6, 107.9, 120.5, 139.1, 145.9, 147.3 (C_6H_3); 159.4, 159.9, 164.4; 166.6 (C-2, C-4, C-7, C-8a); 166.7 (CO). MS (DEI): 466 (M^+, 8); 423 (19); 345 (100). Anal. Calcd. for $C_{25}H_{30}N_4O_5$: C, 64.36; H, 6.48; N, 12.01. Found C, 64.47; H, 6.30; N, 11.87.

Ethyl 2-dimethylamino-7-methyl-5-(3,4-methylendioxyphenyl)-4-morpholino-5H-pyrano[2,3-d]pyrimidin-6-carboxylate ***5o*** (68 %); mp 180-182 °C. IR (KBr): 1710 (CO). ^1H NMR δ ($CDCl_3$): 1.27 (t, 3H, J = 7.1 Hz, CH_2CH_3); 2.44 (s, 3H, CH_3); 3.12 (s, 6H, NMe_2); 3.14-3.24 (m, 2H); 3.35-3.47 (m, 2H); 3.64-3.77 (m, 4H); 4.18 (q, 2H, J = 7.1 Hz, CH_2O); 4.89 (s, 1H, H-5); 5.88 (s, 2H, OCH_2O); 6.64 (s, 3H, C_6H_3). ^{13}C NMR δ ($CDCl_3$): 14.0 (CH_2CH_3); 19.3 (CH_3); 36.7 (NMe_2); 37.0 (C-5); 49.1 (NCH_2); 60.4 (CH_2O); 66.5 (OCH_2); 91.3 (C-4a); 100.7 (OCH_2O); 109.0 (C-6); 107.5, 107.8, 120.5, 138.6, 146.0, 147.3 (C_6H_3); 158.7, 159.8, 164.4; 165.8 (C-2, C-4, C-7, C-8a); 166.5 (CO). MS (DEI): 468 (M^+, 30); 423 (9); 347 (100). Anal. Calcd. for $C_{24}H_{28}N_4O_6$: C, 61.53; H, 6.02; N, 11.96. Found C, 61.41; H, 6.13; N, 12.14.

Ethyl 4-(4-benzylpiperazino)-2-dimethylamino-7-methyl-5-(3,4-methylendioxyphenyl)-5H-pyrano[2,3-d]pyrimidin-6-carboxylate ***5p*** (53 %); mp 170-171 °C. IR (KBr): 1700 (CO). ^1H NMR δ ($CDCl_3$): 1.27 (t, 3H, J = 7.1 Hz, CH_2CH_3); 2.44 (s, 3H, CH_3); 2.49-2.58 (m, 4H, NCH_2); 3.11 (s, 6H, NMe_2); 3.20-3.28 (m, 2H); 3.41-3.53 (m, 2H); 3.53 (s, 2H, NCH_2Ph); 4.16 (q, 2H, J = 7.1 Hz, CH_2O); 4.90 (s, 1H, H-5); 5.87 (s, 2H, OCH_2O); 6.59-6.68 (m, 3H, C_6H_3); 7.26-7.34 (m, 5H, C_6H_5). ^{13}C NMR δ ($CDCl_3$): 14.1 (CH_2CH_3); 19.4 (CH_3); 36.8 (NMe_2); 37.2 (C-5); 48.6 (NCH_2); 52.8 (NCH_2); 60.4 (CH_2O); 62.9 ($PhCH_2$);

91.2 (C-4a); 100.7 (OCH_2O); 109.2 (C-6); 107.6, 107.9, 120.6, 127.0, 128.2, 129.1, 137.8, 146.0, 147.4 (C_6H_5, C_6H_3); 159.2, 159.9, 164.5; 165.9 (C-2, C-4, C-7, C-8a); 166.6 (CO). MS (DEI): 557 (M^+, 8); 466 (23); 411 (38). Anal. Calcd. for $C_{31}H_{35}N_5O_5$: C, 66.77; H, 6.33; N, 12.56. Found C, 66.70; H, 6.49; N, 12.41.

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