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An Efficient Iminophosphorane-Mediated Synthesis for Pyrido[3',2':4,5]thieno[3,2-d] pyrimidine Derivatives

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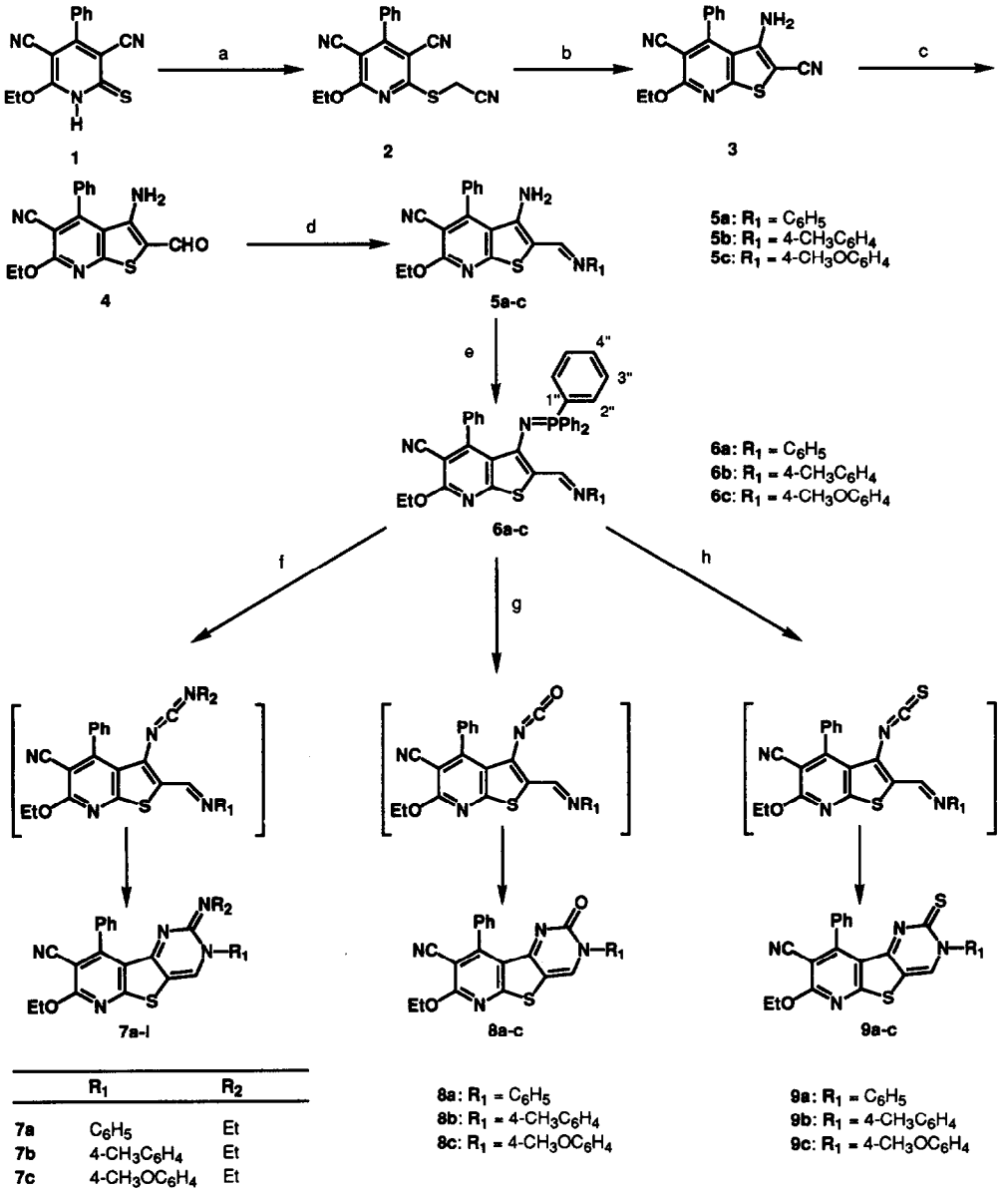
Abstract: A ready one-pot preparation for pyridothienopyrimidines bearing various substituents at position 2 of the pyrimidine ring is reported. The aza Wittig-type reaction of iminophosphoranes derived from the aldehyde **4** with heterocumulenes leads to functionalized fused pyrimidines. Iminophosphoranes **6**, 2-[(N-arylamino)methyl-3-(triphenylphosphoranylidine)amino]thieno[2,3-b]pyridines, react with isocyanates, carbon dioxide and carbon disulfide under mild conditions to give the functionalized 2,3-dihydropyrido[3',2':4,5]thieno[3,2-d]pyrimidines **7**, **8** and **9**, respectively.

The structural diversity and biological significance of fused pyrimidines have aroused much attention in the past few years owing to the wide range of biological activity of these compounds.[1] Many potential drugs have been modelled on them, particularly in cancer and virus research.[2] On the other hand, pyridothienopyrimidines have been the subject of chemical and biological studies on account of their interesting pharmacological properties. A number of syntheses for substituted derivatives of this triheterocyclic ring system, featuring a variety of pharmacological effects have been developed. Such derivatives have analgesic,[3] antipyretic,[4] antianaphilactic[5] and antiinflammatory[6] activity. Also, some are clinically effective antialergic[7] or potentially antineoplastic agents[8], and a few possess significant hypocholesterolemic[9] activity. These assets prompted us to prepare new pyridothienopyrimidines with potential biological activity in our search for novel heterocyclic compounds of pharmacological interest.[10]

Syntheses of fused bi- and polycyclic compounds by annelation of a pyrimidine ring to an existing ring are very numerous and were the subject of recent review.[11] The structure of the required starting compounds is mainly determined by the nature of the substituents on the pyrimidine ring and; as a rule, systems including an amino group next to another functional group are the most widely used in this context.[11] The pyridothienopyrimidine triheterocyclic ring can be synthesized from appropriate pyridothieno derivatives on treatment with one-carbon reagents such as ethyl carbonate, formic acid, esters and orthoesters, amides, urea, cyanates, isothiocyanates, chlorocarbonates, carbon disulfide and thiophosgene.[12]

On the other hand, the aza-Wittig reaction of iminophosphoranes with heterocumulenes, (*e.g.* carbon dioxide, carbon disulfide and isocyanates or isothiocyanates) is a very useful means for synthesizing heterocyclic compounds.[13] Consequently, increased efficiency or expanded applicability are desirable, to which synthesis of functionalized iminophosphoranes bearing a moiety that is able to react with the aza-Wittig product is quite relevant. In this context, the aza-Wittig/electrocyclic ring closure and the aza-Wittig/heterocumulene mediated annulation tandems have proved to be useful protocols for preparing fused

Scheme 1



	R_1	R_2
7a	C_6H_5	Et
7b	4-$CH_3C_6H_4$	Et
7c	4-$CH_3OC_6H_4$	Et
7d	C_6H_5	4-ClC_6H_4
7e	4-$CH_3C_6H_4$	4-ClC_6H_4
7f	4-$CH_3OC_6H_4$	4-ClC_6H_4
7g	C_6H_5	4-FC_6H_4
7h	4-$CH_3C_6H_4$	4-FC_6H_4
7i	4-$CH_3OC_6H_4$	4-FC_6H_4
7j	C_6H_5	4-$CH_3C_6H_4$
7k	4-$CH_3C_6H_4$	4-$CH_3C_6H_4$
7l	4-$CH_3OC_6H_4$	4-$CH_3C_6H_4$

Reagents: a: $ClCH_2CN$, K_2CO_3, acetone, r.t.
b: K_2CO_3, EtOH , reflux
c: DIBAL-H, THF, 0°C
d: H_2NAr, AcOH, EtOH
e: C_2Cl_6, PPh_3, NEt_3, CH_3CN, reflux
f: R_2NCO, toluene, reflux
g: CO_2, toluene, 120°C
h: CS_2, toluene, 120°C

polyheterocyclic systems including the pyrimidine moiety. Molina *et al.* have been especially active in this area, where they have used this cyclization process for the synthesis of a variety of heterocyclic compounds.[14] Analogous methodology has been used to obtain pyrido[1,2-a]pyrimidines, pyrrolo[2,3-d]pyrimidines, pyrimido[4,5-b]azepines and other annelated heterocycles by a suitable choice of (substituted cyclic) iminophosphorane.[15]

In this work, in continuation of our research into the synthesis of pyridothienopyrimidines of biological interest,[10a] we extended application of this method by developing an efficient, ready one-pot synthesis for some derivatives of the pyrido[3',2':4,5]thieno[3,2-d]pyrimidine ring system. The proposed approach involves the aza Wittig-type reaction of iminophosphoranes derived from 3-amino-2-formylthieno[2,3-d]pyridine with heterocumulenes such as carbon dioxide, carbon disulfide and isocyanates or isothiocyanates to give a 1,3,5-hexatriene moiety containing a nitrogen atom at one end and an accumulated double bond at the other, followed by heterocyclization to a functionalized pyrimidine ring.

The starting compound for the aza-Wittig/heterocumulene mediated annulation was prepared from the readily available 3-cyanopyridine-2(1*H*)-thione **1**.[10a] Reaction of this compound **1** with 2-chloroacetonitrile and subsequent base-promoted intramolecular ring formation yielded the 3-aminothieno[2,3-b]pyridine 2-carbonitrile **3** in 80% yield. Regioselective reduction of **3** with diisobutylaluminium hydride leads to the aldehyde **4** in a 80% yield. The structure of compound **4** was determined from microanalyses and spectral data. The mass spectra showed the expected molecular ion peak and the IR spectra exhibited one strong absorption band at $\nu = 1640$ cm^{-1} due to the carbonyl group. Formation of the desired aldehyde **4** was also confirmed by ^{1}H NMR [$\delta = 9.49$ (s, CHO)] and decoupled ^{13}C NMR spectra [$\delta = 183.4$ (CO)].

Treatment of compound **4** with aromatic primary amines in the presence of acetic acid in refluxing ethanol leads to the corresponding aldimines **5** in high yields. The desired key intermediates iminophosphoranes **6** were obtained very readily from **5** by treatment with the triphenylphosphine/triethylamine/hexachloroethane system in dry acetonitrile. Reaction of iminophosphoranes **6** with several isocyanates in refluxing toluene resulted in the formation of triphenylphosphine oxide and the corresponding triheterocyclic 2,3-dihydropyrido[3',2':4,5] thieno[3,2-d]pyrimidine **7** directly in moderate yields. The mechanism for these conversions involves an initial aza-Wittig reaction between the iminophosphorane and the isocyanate to give a carbodiimide that is a highly reactive intermediate[16] and undergoes ready electrocyclic ring-closure to give the cyclic valence tautomers 2,3-dihydropyrido[3',2':4,5]thieno[3,2-d]pyrimidine derivatives **7**. Structural elucidation of compounds **7** was accomplished from their analytical and spectral data. The mass spectra showed the expected molecular ion peaks and the IR spectra exhibited a strong band at $\nu = 1640$-1630 cm^{-1} due to the imino group. The most salient features of the ^{1}H NMR and ^{13}C NMR spectra are summarized under Experimental.

Heating iminophosphoranes **6** in sealed tube at 120°C with carbon dioxide or carbon disulfide in toluene gave rise to the fused pyrimidines **8** and **9** respectively. Similarly, the formation of **8** and **9** can be understood to occur by initial aza-Wittig reaction between iminophosphoranes **6** and carbon dioxide or carbon disulfide to give the corresponding isocyanate or isothiocyanate as intermediates;[17] these last cyclize spontaneously to **8** and **9**, respectively. Compounds **8** and **9** were characterized from their spectroscopic data and mass spectrometric data.

This synthetic approach may be useful in view of the pharmacological interest in this compound class and shows that the aza-Wittig-heterocumulene-mediated annulation strategy tandem affords a new, general route to pyridothienopyrimidines bearing various substituents (alkyl or arylimino, carbonyl, thiocarbonyl) at position 2 of the pyrimidine ring. Even though, there are many available methods for synthesizing pyridothienopyrimidines, to our knowledge, this is the first example of annelation of a pyrimidine ring to an existing pyridothieno system based on the aza-Wittig reaction of iminophosphoranes with heterocumulenes. 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 this triheterocyclic ring system.

EXPERIMENTAL PART

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. ^1H 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.

3,5-Dicyano-2-cyanomethylthio-6-ethoxy-4-phenylpyridine (2):

To a solution of **1** (2.50 g, 8.89 mmol), K_2CO_3 (1.47, 9.44 mmol) and a catalytic amount of KI in acetone (100 mL) was added chloroacetonitrile (1.47 g, 9.05 mmol). The reaction mixture was stirred at room temperature for 18 h. The solvent was removed under reduced pressure and the residual solid was purified by medium-pressure chromatography. Elution with CH_2Cl_2 afforded **2** (2.35 g, 82%); mp 137-138°C. IR (KBr): 2230 (CN); 2220 (CN); 2210 (CN); 1550; 1450; 1350. ^1H NMR δ (CCl_3D): 1.54 (t, 3H, J = 7.1 Hz, CH_3); 3.95 (s, 2H, SCH_2); 4.73 (q, 2H, J = 7.1 Hz, CH_2O); 7.52-7.60 (m, 5H, C_6H_5). ^{13}C NMR δ: ($CDCl_3$): 14.2 ($OCH_2\underline{C}H_3$); 16.4 (SCH_2); 65.7 (OCH_2); 93.7, 99.8 (C-3, C-5); 113.0, 113.3, 115.4 (CN); 128.7, 129.1, 131.3, 132.0 (Py$\underline{C}_6H_5$); 159.8 (C-2); 164.0, 164.7 (C-4, C-6). MS (DEI): 320 (M^+, 39); 292 (34); 291 (100). Anal. Calcd. for $C_{17}H_{12}N_4OS$: C, 63.73; H, 3.78; N, 17.49. Found C, 63.82; H, 3.93; N, 17.20.

3-Amino-2,5-dicyano-6-ethoxy-4-phenylthieno[2,3-b]pyridine (3):

A solution of **2** (1.0 g, 3.12 mmol) and K_2CO_3 (0.60 g, 4.37 mmol) in ethanol (25 mL) was refluxed for 15 min. The solid was filtered off and recrystallized from ethanol/acetone to give **3** (0.98 g, 98%); mp 189-191 °C. IR (KBr): 3500 (NH); 3350 (NH); 2220 (CN); 2210 (CN); 1650. ^1H NMR δ (CCl_3D): 1.55 (t, 3H, J = 7.1 Hz, CH_3); 4.29 (br s, 2H, exchangeable with D_2O, NH_2); 4.60 (q, 2H, J = 7.1 Hz, CH_2O); 7.40-7.63 (m, 5H, C_6H_5). ^{13}C NMR δ (CCl_3D): 14.2 (CH_3); 64.6 (OCH_2); 75.8 (C-2); 96.3 (C-5); 113.7, 114.4 (CN); 115.4 (C-3a); 128.2, 129.5, 130.8, 132.5 (Py$\underline{C}_6H_5$); 149.0 (C-3); 153.3 (C-7a); 163.0, 163.2 (C-4, C-6). MS (DEI): 320 (M^+, 74); 292 (100); 264 (4). Anal. Calcd. for $C_{17}H_{12}N_4OS$: C, 63.73; H, 3.78; N, 17.49. Found C, 63.75; H, 3.90; N, 17.35.

3-Amino-5-cyano-7-ethoxy-2-formyl-4-phenylthieno[2,3-b]pyridine (4):

To an ice-cooled solution of **3** (2.0 g, 6.25 mmol) in dry THF (65 mL) diisobutylaluminium hydride (5 mL, 1.5 M in toluene, 7.5 mmol) was added dropwise. The reaction mixture was stirred under Ar for 2 h and then H_2SO_4 (25 mL, 25%) was added. The reaction mixture was allowed to stand overnight at room temperature. The mixture was extracted with dichloromethane (3 X 20 mL), the organic layers were washed with Na_2CO_3 and dried over Na_2SO_4. The solvent was evaporated under reduced pressure, and the resulting solid was recrystallized from EtOH to afford **3** (1.61 g, 80%); mp 225-227 °C. IR (KBr): 3460 (NH); 3320 (NH); 2220 (CN); 1640 (CO); 1590; 1550; 1340. ^1H NMR δ (CCl_3D): 1.42 (t, 3H, J = 7.1 Hz, CH_3); 4.54 (q, 2H, J = 7.1 Hz, CH_2O); 6.18 (br s, 2H, exchangeable with D_2O, NH_2); 7.11-7.49 (m, 5H, C_6H_5). ^{13}C NMR δ (CCl_3D): 14.2 (CH_3); 64.5 (OCH_2); 95.7 (C-5); 106.4 (C-2); 113.9 (CN); 116.4 (C-3a); 127.8, 129.5, 130.7, 132.5 (Py$\underline{C}_6H_5$); 148.3 (C-3); 154.7 (C-7a); 163.0, 165.7 (C-4, C-6); 183.4 (CO). MS (DEI): 323 (M^+, 100); 294 (90); 267 (25). Anal. Calcd. for $C_{17}H_{13}N_3O_2S$: C, 63.14; H, 4.05; N, 12.99. Found C, 63.23; H, 4.17; N, 12.83.

3-Amino-2-[(N-arylimino)methyl]-5-cyano-6-ethoxy-4-phenylthieno[2,3-b]pyridines 5a-c; General Procedure.

A solution of **4** (4.64 mmol), appropriate aromatic amine (4.64 mmol) and acetic acid (5 mL) in EtOH (75 mL) was refluxed for 3.5 h. After cooling, the precipitate was filtered off and purified by medium-pressure chormatography. Elution with CH_2Cl_2:hexanes (3:2) afforded **5**. The following derivatives **5** were obtained:

3-Amino-5-cyano-6-ethoxy-4-phenyl-2-[(N-phenylimino)methyl]thieno[2,3-b]pyridine ***5a:*** (80 %); mp 242-244 °C. IR (KBr): 3460, 3280 (NH); 2220 (CN); 1600; 1550; 1470. ^{1}H NMR δ (CCl_3D): 1.51 (t, 3H, J = 7.1 Hz, CH_3); 4.62 (q, 2H, J = 7.1 Hz, CH_2O); 6.30 (br s, 2H, NH_2); 7.10-7.63 (m, 10H, C_6H_5); 8.44 (s,1H, CH=N). ^{13}C NMR δ (CCl_3D): 14.4 (CH_3); 64.2 (CH_2O); 95.1 (C-5); 104.5 (C-2); 114.5 (CN); 117.8 (C-3a); 120.7 (C-2'); 125.4 (C-4'); 129.2 (C-3'); 128.1, 129.3, 130.4, 133.7 (PyC_6H_5); 143.5 (C-3); 151.5 (C-1'); 153.1 (C-7a); 153.9 (HC=N); 161.9, 163.9 (C-4, C-6). MS (DEI): 398 (M^+, 100); 369 (64); 266 (16). Anal. Calcd. for $C_{23}H_{18}N_4OS$: C, 69.33; H, 4.55; N, 14.06. Found C, 69.21; H, 4.39; N, 14.21.

3-Amino-5-cyano-6-ethoxy-4-phenyl-2-[(N-p-tolylimino)methyl]thieno[2,3-b]pyridine ***5b***: (84 %); mp 253-255 °C. IR (KBr): 3460, 3240 (NH); 2220 (CN); 1600; 1550; 1480. ^{1}H NMR δ (CCl_3D): 1.51 (t, 3H, J = 7.1 Hz, $CH_2C\underline{H}_3$); 2.34 (s, 3H, CH_3); 4.61 (q, 2H, J = 7.1 Hz, CH_2O); 6.28 (br s, 2H, NH_2); 7.01-7.64 (m, 9H, H_{arom}); 8.43 (s,1H, CH=N). ^{13}C NMR δ (CCl_3D): 14.4 ($CH_2\underline{C}H_3$); 20.3 (CH_3); 64.1 (CH_2O); 95.0 (C-5); 104.6 (C-2); 114.5 (CN); 117.8 (C-3a); 120.5 (C-2'); 129.8 (C-3'); 128.1, 129.3, 130.3, 133.2 (PyC_6H_5); 135.2 (C-4'); 143.2 (C-3); 148.9 (C-1'); 153.0 (C-7a); 153.1 (HC=N); 161.8, 163.8 (C-4, C-6). MS (DEI): 412 (M^+, 9); 383 (4). Anal. Calcd. for $C_{24}H_{20}N_4OS$: C, 69.88; H, 4.89; N, 13.58. Found C, 69.84; H, 4.88; N, 13.37.

3-Amino--5-cyano-6-ethoxy-4-phenyl-2-[(N-p-methoxyphenylmino)methyl]lthieno[2,3-b] pyridine ***5c***: (89 %); mp 234-236 °C. IR (KBr): 3460 (NH); 2220 (CN); 1595; 1540. ^{1}H NMR δ (CCl_3D): 1.50 (t, 3H, J = 7.1 Hz, CH_3); 3.80 (s, 3H, OCH_3); 4.60 (q, 2H, J = 7.1 Hz, CH_2O); 6.24 (br s, 2H, NH_2); 6.87, 7.08 (AB system, 4H, J = 8.8 Hz, $C_6\underline{H}_4OCH_3$); 7.45-7.64 (m, 5H, C_6H_5); 8.42 (s,1H, CH=N). ^{13}C NMR δ (CCl_3D): 14.4 (CH_3); 55.5 (OCH_3); 64.1 (CH_2O); 95.0 (C-5); 104.8 (C-2); 114.4 (C-3'); 114.5 (CN); 117.9 (C-3a); 121.6 (C-2'); 128.1, 129.2, 130.3, 133.3 ($Py\underline{C}_6H_5$); 142.9 (C-3); 144.6 (C-1'); 152.1 (HC=N); 152.9 (C-7a); 157.7 (C-4'); 161.7, 163.7 (C-4, C-6). MS (DEI): 428 (M^+, 24); 399 (7). Anal. Calcd. for $C_{24}H_{20}N_4O_2S$: C, 67.27; H, 4.70; N, 13.08. Found C, 67.51; H, 4.74; N, 13.14.

2-[(N-arylimino)methyl]-5-cyano-6-ethoxy-4-phenyl-3[(triphenylphophoranyldene)amino] thieno[2,3-b]pyridines 6a-c; General Procedure.

To a solution of the appropriate imine **5** (3.19 mmol) in dry acetonitrile (90 mL) were added triphenylphosphine (0.84 g, 3.19 mmol), triethylamine (0.57 g, 5.58 mmol) and hexachloroethane (0.76 g, 3.19 mmol). The reaction mixture was heated under reflux with stirring in an argon atmosphere for 3h. After cooling, the resulting solid was filtered off and recrystallized from EtOH/CH_2Cl_2 to give **6**. The following derivatives **6** were obtained:

5-Cyano-6-ethoxy-4-phenyl-2-[(N-phenylimino)methyl]-3[(triphenylphophoranyldene)amino]thieno[2,3-b] pyridine ***6a***: (70 %); mp 210-212 °C. ^{1}H NMR δ (CCl_3D): 1.48 (t, 3H, J = 7.1 Hz, CH_3); 4.60 (q, 2H, J = 7.1 Hz, CH_2O); 6.51-7.42 (m, 25H, C_6H_5); 8.03 (s, 1H, CH=N). ^{13}C NMR δ (CCl_3D): 14.4 (CH_3); 63.7 (OCH_2); 95.2 (C-5); 115.5 (CN); 119.3 (d, J = 5.9 Hz, C-3a); 121.0 (C-2'); 124.6 (C-2); 124.7 (C-4'); 127.6 (C-3'); 128.4, 128.7, 129.1, 135.4 ($Py\underline{C}_6H_5$); 128.6 (d, J = 12 Hz, C-3"); 129.0 (d, J = 102 Hz, C-1"); 131.9 (d, J = 2.7 Hz, C-4"); 132.2 (d, J = 10 Hz, C-2"); 148.6 (C-3); 151.9 (C-1'); 153.9 (HC=N); 162.2, 164.2 (C-4, C-6). MS (FAB): 659 [$(MH)^+$, 100]; 631 (10); 584 (13); 262 (18); 183 (72). Anal. Calcd. for $C_{41}H_{31}N_4OPS$: C, 74.76; H, 4.74; N, 8.51. Found C, 74.90; H, 4.66; N, 8.47.

5-Cyano-6-ethoxy-4-phenyl-2-[(N-tolylimino)methyl]-3[(triphenylphophoranyldene)amino]thieno[2,3-b]pyridine ***6b*** (82 %); mp 269-271 °C. ^{1}H NMR δ (CCl_3D): 1.48 (t, 3H, J = 7.1 Hz, $CH_2\underline{CH_3}$); 2.28 (s, 3H, CH_3); 4.60 (q, 2H, J = 7.1 Hz, CH_2O); 6.44, 6.90 (AB system, 4H, J = 8.2 Hz, $C_6\underline{H_4}OCH_3$); 7.14-7.43 (m, 20H, C_6H_5); 8.07 (s,1H, CH=N). ^{13}C NMR δ (CCl_3D): 14.4 ($OCH_2\underline{C}H_3$); 20.9 (CH_3); 63.7 (OCH_2); 95.2 (C-5); 115.5 (CN); 119.8 (C-3a); 121.0 (C-2'); 127.6 (C-3'); 128.7, 129.0, 129.2, 135.4 ($Py\underline{C}_6H_5$); 128.8 (d, J = 12 Hz, C-3"); 131.9 (d, J = 2.7 Hz, C-4"); 132.2 (d, J = 10 Hz, C-2"); 134.4 (C-4'); 148.2 (C-3); 149.0 (C-1'); 152.8 (HC=N); 153.7 (C-7a); 162.2, 164.3 (C-4, C-6). MS (FAB): 673 [$(MH)^+$, 100]; 645 (11); 568 (15); 262 (29); 183 (75). Anal. Calcd. for $C_{42}H_{33}N_4OPS$: C, 74.98; H, 4.94; N, 8.33. Found C, 74.76; H, 4.96; N, 8.44.

5-Cyano-6-ethoxy-4-phenyl-2-[(N-methoxyphenylimino)methyl]-3-[(triphenylphophoranyldene)amino]thieno [2,3-b]pyridine ***6c*** (68 %); mp 254-256 °C. ^{1}H NMR δ (CCl_3D): 1.48 (t, 3H, J = 7.1 Hz, CH_3); 3.78 (s, 3H, OCH_3); 4.61 (q, 2H, J = 7.1 Hz, CH_2O); 6.52, 6.67 (AB system, 4H, J = 8.9 Hz, $C_6\underline{H_4}OCH_3$); 7.14-7.47 (m, 20H, C_6H_5); 8.05 (s, 1H, CH=N). ^{13}C NMR δ (CCl_3D): 14.4 ($OCH_2\underline{C}H_3$); 55.3 (OCH_3); 63.7 (OCH_2); 95.1 (C-5); 113.6 (C-3'); 115.5 (CN); 119.6 (d, J = 6.3 Hz, C-3a); 122.0 (C-2'); 124.4 (d, J = 6.1 Hz, C-2); 127.6, 128.6, 129.1, 135.4 ($Py\underline{C}_6H_5$); 128.7 (d, J = 12 Hz, C-3"); 131.8 (d, J = 2.7 Hz, C-4"); 132.2 (d, J = 10 Hz, C-2"); 145.0 (C-1'); 147.7 (C-3); 152.2 (HC=N); 153.7 (C-7a); 157.2 (C-4'); 162.0, 164.0 (C-4, C-6). MS (FAB): 689 [$(MH)^+$, 86]; 674 (64); 568 (23); 262 (42), 183 (100). Anal. Calcd. for $C_{42}H_{33}N_4O_2PS$: C, 73.24; H, 4.83; N, 8.13. Found C, 72.99; H, 4.89; N, 8.21.

8-Cyano-7-ethoxy-9-phenyl-3-aryl-2-(ethyl or arylimino)-2,3-dihydropyrido[3",2":4',5'] thieno[3,2-d]pyrimidines 7; General Procedure.

A solution of the appropriate isocyanate (0.4 mmol) in dry toluene (1 mL) was added to a solution of iminophosphorane **6** (0.30 mmol) in dry toluene (10 mL). The reaction mixture was heated under reflux with stirring in an argon atmosphere for 4h. Upon cooling, the solvent was removed under reduced pressure and ether (20 mL) was added. The solid was filtered off and recrystallized from acetonitrile to give **7**. The following derivatives **7** were obtained:

8-Cyano-7-ethoxy-2-ethylimino-3,9-diphenyl-2,3-dihydropyrido[3",2":4',5']thieno[3,2-d]pyrimidine ***7a*** (52 %); mp 260-262 °C. IR (KBr): 2220 (CN); 1630; 1590; 1540; 1340. ^{1}H NMR δ (CCl_3D): 1.44 (t, 3H, J = 7.1 Hz, CH_3); 1.50 (t, 3H, J = 7.1 Hz, CH_3); 4.02 (q, 2H, J = 7.1 Hz, CH_2N); 4.62 (q, 2H, J = 7.1 Hz, CH_2O); 6.64-7.30 (m, 10H, C_6H_5); 7.74 (s, 1H, H-4). ^{13}C NMR δ (CCl_3D): 13.6 ($NCH_2\underline{C}H_3$); 14.4 ($OCH_2\underline{C}H_3$); 48.7 (NCH_2); 63.7 (OCH_2); 96.3 (C-8); 107.2 (C-4a); 114.3 (CN); 117.4 (C-9a); 121.0 (C-2'); 122.4 (C-4'); 127.9 (C-3'); 128.4, 128.6, 130.4, 132.0 ($Py\underline{C}_6H_5$); 140.7 (C-4); 147.7 (C-1'); 148.5 (C-9b); 156.8 (C-5a); 162.3 (C-2); 165.1, 170.5 (C-7, C-9). MS (FAB): 451 [$(MH)^+$, 100]; 423 (14); 287 (17). Anal. Calcd. for $C_{26}H_{21}N_5OS$: C, 69.16; H, 4.69; N, 15.51. Found C, 69.29; H, 4.83; N, 15.26.

8-Cyano-7-ethoxy-2-ethylimino-9-phenyl-3-tolyl-2,3-dihydropyrido[3",2":4',5']thieno[3,2-d]pyrimidine ***7b*** (52 %); mp 255-257 °C. IR (KBr): 2220 (CN); 1640; 1590; 1540; 1490; 1340. ^{1}H NMR δ (CCl_3D): 1.43 (t, 3H, J = 7.1 Hz, CH_3); 1.49 (t, 3H, J = 7.1 Hz, CH_3); 2.32 (s, 3H, $C_6H_4C\underline{H_3}$).3.99 (q, 2H, J = 7.1 Hz, CH_2N); 4.60 (q, 2H, J = 7.1 Hz, CH_2O); 6.53, 6.78 (AB system, 4H, J = 8.2, C_6H_4); 7.12-7.30 (m, 5H, C_6H_5); 7.71 (s, 1H, H-4). MS (FAB): 466 [$(MH)^+$, 100]; 438 (31); 410 (22); 408 (26). Anal. Calcd. for $C_{27}H_{23}N_5OS$: C, 69.66; H, 4.98; N, 15.04. Found C, 69.39; H, 4.82; N, 15.09.

8-Cyano-7-ethoxy-2-ethylimino-9-phenyl-3-(4-methoxyphenyl)-2,3-dihydropyrido[3",2":4',5']thieno[3,2-d] pyrimidine ***7c*** (55 %); mp 255-257 °C. IR (KBr): 2220 (CN); 1630; 1540; 1490; 1340. ^{1}H NMR δ (CCl_3D): 1.43 (t, 3H, J = 7.1 Hz, CH_3); 1.50 (t, 3H, J = 7.1 Hz, CH_3); 3.82 (s, 3H, $C_6H_4OC\underline{H_3}$).3.99 (q, 2H, J = 7.1 Hz, CH_2N); 4.62 (q, 2H, J = 7.1 Hz, CH_2O); 6.52-6.54 (m, 4H, C_6H_4); 7.20-7.34 (m, 5H, C_6H_5); 7.70

(s, 1H, H-4). MS (FAB): 482 [(MH)$^+$, 100]; 454 (31); 426 (17); 410 (24). Anal. Calcd. for $C_{27}H_{23}N_5O_2S$: C, 67.34; H, 4.81; N, 14.54. Found C, 67.39; H, 4.59; N, 14.65.

2-(4-Chlorophenylimino)-8-cyano-7-ethoxy-3,9-diphenyl-2,3-dihydropyrido[3'',2'':4',5']thieno[3,2-d] pyrimidine ***7d*** (50 %); mp 182-184 °C. IR (KBr): 2220 (CN); 1630; 1550; 1480; 1340. ^{1}H NMR δ (CCl_3D): 1.52 (t, 3H, J = 7.1 Hz, CH_3); 4.64 (q, 2H, J = 7.1 Hz, CH_2O); 6.45, 6.86 (AB system, 4H, J = 8.7, C_6H_4Cl); 7.23-7.54 (m, 10H, C_6H_5); 7.73 (s, 1H, H-4). ^{13}C NMR δ (CCl_3D): 14.4 (CH_3); 65.1 (OCH_2); 96.7 (C-8); 108.3 (C-4a); 114.3 (CN); 117.2 (C-9a); 123.7 (C-2''); 126.0 (C-4''); 126.6 (C-2'); 128.1, 128.4, 130.5, 132.1 (Py$\underline{C}_6H_5$); 128.5 (C-3''),128.8 (C-3'); 129.7 (C-4'); 141.5 (C-4); 142.5 (C-1'); 147.2 (C-1''); 149.5 (C-9b); 157.2 (C-5a); 163.3 (C-2); 165.5, 171.4 (C-7, C-9). MS (FAB): 536 [(MH)$^+$+2, 47)]; 534 [(MH)$^+$, 100]; 506 (71); 470 (14); 301 (31). Anal. Calcd. for $C_{30}H_{20}ClN_5OS$: C, 67.47; H, 3.78; N, 13.11. Found C, 67.53; H, 3.60; N, 12.90.

2-(4-Chlorophenylimino)-8-cyano-7-ethoxy-9-phenyl-3-tolyl-2,3-dihydropyrido[3'',2'':4',5']thieno[3,2-d] pyrimidine ***7e*** (50 %); mp 252-254 °C. IR (KBr): 2220 (CN); 1630; 1540; 1480; 1320. ^{1}H NMR δ (CCl_3D): 1.51 (t, 3H, J = 7.1 Hz, $CH_2C\underline{H}_3$); 2.38 (s, 3H, CH_3); 4.62 (q, 2H, J = 7.1 Hz, CH_2O); 6.44, 6.86 (AB system, 4H, J = 8.6, $C_6\underline{H}_4Cl$); 7.14-7.46 (m, 9H, H_{arom}); 7.71 (s, 1H, H-4). ^{13}C NMR δ (CCl_3D): 14.3 ($CH_2\underline{C}H_3$); 21.2 (CH_3); 64.9 (OCH_2); 96.5 (C-8); 108.1 (C-4a); 114.2 (CN); 130.1 (C-3'); 117.1 (C-9a); 123.6 (C-2''); 125.8 (C-4''); 126.2 (C-2'); 128.3, 128.4, 130.3, 131.9 (Py$\underline{C}_6H_5$); 127.9 (C-3''), 138.7 (C-1'); 141.5 (C-4); 147.2 (C-1''); 149.6 (C-9b); 157.0 (C-5a); 163.1 (C-2); 165.4, 171.2 (C-7, C-9). MS (FAB): 549 (M$^+$+2, 47); 547 (M$^+$, 100),519 (27). Anal. Calcd. for $C_{31}H_{22}ClN_5OS$: C, 67.94; H, 4.05; N, 12.78. Found C, 67.76; H, 4.17; N, 12.91.

2-(4-Chlorophenylimino)-8-cyano-7-ethoxy-3-(4-methoxyphenyl)-9-phenyl-2,3-dihydropyrido[3'',2'':4',5'] thieno[3,2-d]pyrimidine ***7f*** (56 %); mp 195-197 °C. IR (KBr): 2220 (CN); 1620; 1540; 1500; 1470; 1340. ^{1}H NMR δ (CCl_3D): 1.51 (t, 3H, J = 7.1 Hz, $CH_2C\underline{H}_3$); 3.83 (s, 3H, OCH_3); 4.63 (q, 2H, J = 7.1 Hz, CH_2O); 6.45, 6.86 (AB system, 4H, J = 8.7, $C_6\underline{H}_4Cl$); 6.96, 7.35 (AB system, 4H, J = 8.9, $C_6\underline{H}_4OCH_3$); 7.14-7.60 (m, 5H, C_6H_5); 7.73 (s, 1H, H-4). ^{13}C NMR δ (CCl_3D): 14.3 ($CH_2\underline{C}H_3$); 55.5 (OCH_3); 64.9 (OCH_2); 96.6 (C-8); 108.1 (C-4a); 114.2 (CN); 114.7 (C-3'); 117.1 (C-9a); 123.6 (C-2''); 125.8 (C-4''); 126.6 (C-2'); 128.3, 128.4, 130.3 (Py$\underline{C}_6H_5$); 128.5 (C-2'), 128.6 (C-3''); 135.0 (C-1'); 141.7 (C-4); 147.2 (C-1''); 149.7 (C-9b); 157.0 (C-5a); 163.0 (C-2); 165.4, 171.3 (C-7, C-9). MS (FAB): 565 (M$^+$+2, 47); 563 (M$^+$, 98), 535 (21), 278 (100). Anal. Calcd. for $C_{31}H_{22}ClN_5O_2S$: C, 66.01; H, 3.93; N, 12.42. Found C, 66.19; H, 3.90; N, 12.20.

8-Cyano-7-ethoxy-2-(4-fluorphenylimino)-3,9-diphenyl-2,3-dihydropyrido[3'',2'':4',5']thieno[3,2-d] pyrimidine ***7g*** (52 %); mp 254-256 °C. IR (KBr): 2220 (CN); 1630; 1600; 1540; 1490; 1380; 1340. ^{1}H NMR δ (CCl_3D): 1.52 (t, 3H, J = 7.1 Hz, CH_3); 4.64 (q, 2H, J = 7.1 Hz, CH_2O); 6.45-7.51 (m, 14H, H_{arom}); 7.69 (s, 1H, H-4). ^{13}C NMR δ (CCl_3D): 14.3 (CH_3); 64.9 (OCH_2); 96.5 (C-8); 107.8 (C-4a); 114.2 (CN); 114.8 (d, J = 21 Hz, C-3''); 117.1 (C-9a); 123.3 (d, J = 7 Hz, C-2''); 126.5 (C-2'); 128.0, 128.4, 130.2, 132.1 (Py$\underline{C}_6H_5$); 129.4 (C-3'); 130.4 (C-4'); 141.5 (C-4); 142.4 (C-1'); 144.2 (C-1''); 149.1 (C-9b); 156.9 (C-5a); 158.4 (d, J = 237 Hz, C-4''); 163.0 (C-2); 165.3, 171.2 (C-7, C-9). MS (FAB): 518 [(MH)$^+$, 100]; 490 (71). Anal. Calcd. for $C_{30}H_{20}FN_5OS$: C, 69.62; H, 3.90; N, 13.53. Found C, 69.38; H, 3.69; N, 13.35.

8-Cyano-7-ethoxy-2-(4-fluorphenylimino)-9-phenyl-3-tolyl-2,3-dihydropyrido[3'',2'':4',5']thieno[3,2-d] pyrimidine ***7h*** (51 %); mp 252-254 °C. IR (KBr): 2220 (CN); 1630; 1540; 1490; 1370; 1340. ^{1}H NMR δ (CCl_3D): 1.51 (t, 3H, J = 7.1 Hz, $CH_2C\underline{H}_3$); 2.38 (s, 3H, $C_6H_4C\underline{H}_3$); 4.63 (q, 2H, J = 7.1 Hz, CH_2O); 6.42-7.34 (m, 13H, H_{arom}); 7.70 (s, 1H, H-4). ^{13}C NMR δ (CCl_3D): 14.3 ($CH_2\underline{C}H_3$); 21.2 (CH_3); 64.9 (OCH_2); 96.4 (C-8); 107.7 (C-4a); 114.2 (CN); 114.8 (d, J = 22 Hz, C-3''); 117.2 (C-9a); 123.3 (d, J = 8 Hz, C-2''); 126.2 (C-2'); 128.0, 128.2, 130.2, 132.1 (Py$\underline{C}_6H_5$); 130.1 (C-3'); 138.6 (C-1'); 139.9 (C-4');

141.5 (C-4); 144.4 (d, J = 4 Hz, C-1"); 149.3 (C-9b); 156.9 (C-5a); 158.4 (d, J = 238 Hz, C-4"); 163.0 (C-2); 165.3, 171.2 (C-7, C-9). MS (FAB): 532 [(MH)$^+$, 100]; 504 (60). Anal. Calcd. for $C_{31}H_{22}FN_5OS$: C, 70.04; H, 4.17; N, 13.17. Found C, 69.87; H, 4.01; N, 13.31.

8-Cyano-7-ethoxy-2-(4-fluorphenylimino)-3-(4-methoxyphenyl)-9-phenyl-2,3-dihydropyrido[3",2":4',5'] thieno[3,2-d]pyrimidine ***7i*** (65 %); mp 220-222 °C. IR (KBr): 2220 (CN); 1630; 1590; 1540; 1510; 1490. ^{1}H NMR δ (CCl_3D): 1.51 (t, 3H, J = 7.1 Hz, $CH_2C\underline{H}_3$); 3.83 (s, 3H, OCH_3); 4.63 (q, 2H, J = 7.1 Hz, CH_2O); 6.43-7.40 (m, 13H, H_{arom}); 7.71 (s, 1H, H-4). ^{13}C NMR δ (CCl_3D): 14.3 ($CH_2\underline{C}H_3$); 55.5 (OCH_3); 64.9 (OCH_2); 96.5 (C-8); 107.7 (C-4a); 114.2 (CN); 114.6 (C-3'); 114.8 (d, J = 22 Hz, C-3"); 117.2 (C-9a); 123.3 (d, J = 8 Hz, C-2"); 127.6 (C-2'); 128.0, 128.3, 130.2, 132.1 ($Py\underline{C}_6H_5$); 135.2 (C-1'); 141.7 (C-4); 144.4 (C-1"); 149.2 (C-9b); 156.9 (C-5a); 158.4 (d, J = 238 Hz, C-4"); 159.4 (C-4'); 163.0 (C-2); 165.3, 171.1 (C-7, C-9). MS (FAB): 548 [(MH)$^+$, 100]; 520 (75). Anal. Calcd. for $C_{31}H_{22}FN_5O_2S$: C, 67.99; H, 4.05; N, 12.79. Found C, 68.20; H, 4.25; N, 12.58.

8-Cyano-7-ethoxy-3,9-diphenyl-2-tolylmino-2,3-dihydropyrido[3",2":4',5']thieno[3,2-d]pyrimidine ***7j*** (54 %); mp 218-220 °C. IR (KBr): 2220 (CN); 1630; 1590; 1540; 1480; 1340. ^{1}H NMR δ (CCl_3D): 1.51 (t, 3H, J = 7.1 Hz, $CH_2C\underline{H}_3$); 2.38 (s, 3H, CH_3); 4.63 (q, 2H, J = 7.1 Hz, CH_2O); 6.50-7.42 (m, 14H, H_{arom}); 7.73 (s, 1H, H-4). MS (FAB): 514 [(MH)$^+$, 94]; 486 (45). Anal. Calcd. for $C_{31}H_{23}N_5OS$: C, 72.49; H, 4.51; N, 13.64. Found C, 72.29; H, 4.72; N, 13.55.

8-Cyano-7-ethoxy-9-phenyl-3-tolyl-2-tolylimino-2,3-dihydropyrido[3",2":4',5']thieno[3,2-d]pyrimidine ***7k*** (52 %); mp 242-244 °C. IR (KBr): 2220 (CN); 1630; 1540; 1490; 1310. ^{1}H NMR δ (CCl_3D): 1.47 (t, 3H, J = 7.1 Hz, $CH_2C\underline{H}_3$); 2.26 (s, 3H, CH_3); 2.34 (s, 3H, CH_3); 4.60 (q, 2H, J = 7.1 Hz, CH_2O); 6.40, 6.70 (AB system, 4H, J = 8.1 Hz, $C_6\underline{H}_4CH_3$); 7.10-7.31 (m, 9H, H_{arom}); 7.65 (s, 1H, H-4). ^{13}C NMR δ (CCl_3D): 14.3 ($CH_2\underline{C}H_3$); 21.0, 21.2 (CH_3); 64.8 (OCH_2); 96.3 (C-8); 107.4 (C-4a); 114.3 (CN); 117.2 (C-9a); 122.1 (C-2"); 126.2 (C-2'); 127.8, 129.1, 130.7 ($Py\underline{C}_6H_5$); 128.4 (C-3"); 130.0 (C-3'); 132.0 (C-4"); 138.4 (C-1'); 141.5 (C-4); 145.6 (C-1"); 140.8 (C-4'); 148.8 (C-9b); 156.9 (C-5a); 162.9 (C-2); 165.3, 171.2 (C-7, C-9). MS (FAB): 528 [(MH)$^+$, 100]; 500 (66). Anal. Calcd. for $C_{32}H_{25}N_5OS$: C, 72.84; H, 4.78; N, 13.27. Found C, 73.05; H, 4.63; N, 13.08.

8-Cyano-7-ethoxy-3-(4-methoxyphenyl)-9-phenyl-2-tolylimino-2,3-dihydropyrido[3",2":4',5']thieno[3,2-d] pyrimidine ***7l*** (55 %); mp 259-261 °C. IR (KBr): 2220 (CN); 1630; 1540; 1480; 1340. ^{1}H NMR δ (CCl_3D): 1.58 (t, 3H, J = 7.1 Hz, $CH_2C\underline{H}_3$); 2.36 (s, 3H, CH_3); 3.89 (s, 3H, OCH_3); 4.70 (q, 2H, J = 7.1 Hz, CH_2O); 6.50, 6.80 (AB system, 4H, J = 8.1 Hz, $C_6\underline{H}_4CH_3$); 7.01, 7.43 (AB system, 4H, J = 9.0 Hz, $C_6\underline{H}_4OCH_3$); 7.19-7.47 (m, 5H, C_6H_5); 7.75 (s, 1H, H-4). MS (FAB): 544 [(MH)$^+$, 100]; 516 (68). Anal. Calcd. for $C_{32}H_{25}N_5O_2S$: C, 70.70; H, 4.64; N, 12.88. Found C, 70.84; H, 4.41; N, 12.99.

8-Cyano-7-ethoxy-9-phenyl-3-aryl-2-(oxo or thioxo)-2,3-dihydropyrido[3'',2'':4',5'] thieno[3,2-d]pyrimidines 8 and 9;General Procedure.

The iminophosphorane **6** (0.30 mmol); in dry toluene (15 mL) and an excess of solid carbon dioxide or carbon disulfide (2 mL) was heated in sealed tube at 120°C in an argon atmosphere for 12h. After cooling, the solvent was removed under reduced pressure and the crude product was recrystallized from CH_2Cl_2/ether to give **8** or **9**. The following derivatives **8** and **9** were obtained:

8-Cyano-7-ethoxy-3,9-diphenyl-2-oxo-2,3-dihydropyrido[3",2":4',5']thieno[3,2-d]pyrimidine **8a** (62 %); mp >300 °C. IR (KBr): 2220 (CN); 1670 (CO); 1540; 1480; 1420. ^{1}H NMR δ (CCl_3D): 1.53 (t, 3H, J = 7.1 Hz, CH_3); 4.68 (q, 2H, J = 7.1 Hz, CH_2O); 7.37-7.50 (m, 10H, C_6H_5); 8.08 (s, 1H, H-4). ^{13}C NMR δ (CCl_3D): 14.3 (CH_3); 65.1 (OCH_2); 96.7 (C-8); 111.5 (C-4a); 114.1 (CN); 116.9 (C-9a); 126.0 (C-2'); 128.1, 129.0, 130.4, 131.9 ($Py\underline{C}_6H_5$); 129.1 (C-4'); 129.4 (C-3'); 141.9 (C-1'); 140.7 (C-4); 153.9 (C-5a);

157.5 (C-9b); 165.5, 165.9 (C-7, C-9); 171.0 (C-2). MS (FAB): 425 [(MH)$^+$, 100]; 397 (83); 301 (39). Anal. Calcd. for $C_{24}H_{16}N_4O_2S$: C, 67.91; H, 3.80; N, 13.20. Found C, 68.04; H, 3.72; N, 13.09.

8-Cyano-7-ethoxy-9-phenyl-2-oxo-3-tolyl-2,3-dihydropyrido[3'',2'':4',5']thieno[3,2-d]pyrimidine **8b** (57 %); mp 277-279 °C. IR (KBr): 2220 (CN); 1660 (CO); 1540; 1480; 1420. ^{1}H NMR δ (CCl_3D): 1.53 (t, 3H, J = 7.1 Hz, CH_3); 2.36 (s, 3H, $C\underline{H}_3C_6H_4$); 4.67 (q, 2H, J = 7.1 Hz, CH_2O); 7.21 (s, 4H, C_6H_4); 7.48 (s, 5H, C_6H_5); 8.07 (s, 1H, H-4). ^{13}C NMR δ (CCl_3D): 14.3 ($OCH_2\underline{C}H_3$); 21.1 (CH_3); 65.1 (OCH_2); 96.6 (C-8); 111.3 (C-4a); 114.1 (CN); 116.9 (C-9a); 125.7 (C-2'); 128.1, 129.0, 130.3, 131.9 (Py$\underline{C}_6H_5$); 129.9 (C-3'); 138.1 (C-4'); 139.1 (C-1'); 142.3 (C-4); 154.0 (C-5a); 157.0 (C-9b); 165.4, 165.7 (C-7, C-9); 170.9 (C-2). MS (FAB): 438 [(MH)$^+$, 75]; 410 (100); 278 (82). Anal. Calcd. for $C_{25}H_{18}N_4O_2S$: C, 68.48; H, 4.14; N, 12.78. Found C, 68.21; H, 4.16; N, 12.74.

8-Cyano-7-ethoxy-9-phenyl-3-(p-methoxyphenyl)-2-oxo-2,3-dihydropyrido[3'',2'':4',5']thieno[3,2-d] pyrimidine **8c** (81 %); mp 280-282 °C. IR (KBr): 2220 (CN); 1660 (CO); 1540; 1500; 1410. ^{1}H NMR δ (CCl_3D): 1.53 (t, 3H, J = 7.1 Hz, CH_3); 3.80 (s, 3H, OCH_3); 4.67 (q, 2H, J = 7.1 Hz, CH_2O); 6.90, 7.25 (AB system, 4H, J = 9.0 Hz, C_6H_4); 7.49 (s, 5H, C_6H_5); 8.06 (s, 1H, H-4). ^{13}C NMR δ (CCl_3D): 14.3 ($OCH_2\underline{C}H_3$); 55.6 (OCH_3); 65.1 (OCH_2); 96.8 (C-8); 111.3 (C-4a); 114.0 (CN); 114,6 (C-3'); 117.0 (C-9a); 127.2 (C-2'); 128.1, 129.0, 130.3, 132.1 (Py$\underline{C}_6H_5$); 133.6 (C-1'); 142.0 (C-4); 154.1 (C-5a); 157.6 (C-9b); 159.9 (C-4'); 165.5, 165.8 (C-7, C-9); 170.9 (C-2).MS (FAB): 455 [(MH)$^+$, 100]; 427 (93). Anal. Calcd. for $C_{25}H_{18}N_4O_3S$: C, 66.07; H, 3.99; N, 12.33. Found C, 66.30; H, 4.15; N, 12.27.

8-Cyano-7-ethoxy-3,9-diphenyl-2-thioxo-2,3-dihydropyrido[3'',2'':4',5']thieno[3,2-d]pyrimidine **9a** (62 %); mp 228-230 °C. IR (KBr): 2220 (CN); 1560; 1480; 1420. ^{1}H NMR δ (CCl_3D): 1.56 (t, 3H, J = 7.1 Hz, CH_3); 4.70 (q, 2H, J = 7.1 Hz, CH_2O); 7.24-7.57 (m, 10H, C_6H_5); 8.16 (s, 1H, H-4). ^{13}C NMR δ (CCl_3D): 14.3 (CH_3); 65.4 (OCH_2); 97.2 (C-8); 113.9 (CN); 116.1 (C-4a); 116.5 (C-9a); 126.4 (C-2'); 128.1, 129.8, 130.7, 131.5 (Py$\underline{C}_6H_5$); 129.3 (C-4'); 129.5 (C-3'); 142.6 (C-4); 144.3 (C-1'); 157.7 (C-5a); 159.8 (C-9b); 165.8, 171.0 (C-7, C-9); 179.8 (C-2). MS (FAB): 441 [(MH)$^+$,100]; 413 (71); 301 (14). Anal. Calcd. for $C_{24}H_{16}N_4OS_2$: C, 65.44; H, 3.66; N, 12.72. Found C, 65.25; H, 3.59; N, 12.55.

8-Cyano-7-ethoxy-9-phenyl-2-thioxo-3-tolyl-2,3-dihydropyrido[3'',2'':4',5']thieno[3,2-d]pyrimidine **9b** (75 %); mp 218-220 °C. IR (KBr): 2220 (CN); 1600; 1540; 1480; 1340. ^{1}H NMR δ (CCl_3D): 1.56 (t, 3H, J = 7.1 Hz, $CH_2C\underline{H}_3$); 2.23 (s, 3H, $C_6H_4C\underline{H}_3$); 4.70 (q, 2H, J = 7.1 Hz, CH_2O); 7.03 (s, 4H, C_6H_4); 7.50 (s, 5H, C_6H_5); 8.11 (s, 1H, H-4). ^{13}C NMR δ (CCl_3D): 14.2 ($OCH_2\underline{C}H_3$); 21.1 (CH_3); 65.3 (OCH_2); 96.6 (C-8); 115.8 (C-4a); 114.0 (CN); 116.9 (C-9a); 125.9 (C-2'); 127.8, 129.9, 130.7, 131.2 (Py$\underline{C}_6H_5$); 129.5 (C-3'); 139.4 (C-4'); 141.4 (C-1'); 143.9 (C-4); 157.0 (C-5a); 159.2 (C-9b); 165.5, 171.1 (C-7, C-9); 179.2 (C-2). MS (FAB): 455 [(MH)$^+$,100]; 427 (86); 395 (18); 299 (20). Anal. Calcd. for $C_{25}H_{18}N_4OS_2$: C, 66.06; H, 3.99; N, 12.33. Found C, 65.82; H, 3.91; N, 12.31.

8-Cyano-7-ethoxy-9-phenyl-3-(p-methoxyphenyl)-2-thioxo-2,3-dihydropyrido[3'',2'':4',5']thieno[3,2-d] pyrimidine **9c** (88 %); mp 220-222 °C. IR (KBr): 2220 (CN); 1600; 1540; 1500; 1340. ^{1}H NMR δ (CCl_3D): 1.55 (t, 3H, J = 7.1 Hz, CH_3); 3.85 (s, 3H, OCH_3); 4.69 (q, 2H, J = 7.1 Hz, CH_2O); 6.99, 7.24 (AB system, 4H, J = 8.9 Hz, C_6H_4); 7.52-7.61 (m, 5H, C_6H_5); 8.18 (s, 1H, H-4). ^{13}C NMR δ (CCl_3D): 14.2 ($OCH_2\underline{C}H_3$); 55.5 (OCH_3); 65.0 (OCH_2); 96.2 (C-8); 114.3 (CN); 114,4 (C-3'); 116.0 (C-4a); 116.2 (C-9a); 127.7 (C-2'); 128.0, 129.2, 129.9, 132.2 (Py$\underline{C}_6H_5$); 137.7 (C-1'); 146.3 (C-4); 156.5 (C-5a); 158.8 (C-4'); 159.2 (C-9b); 164.9, 170.6 (C-7, C-9); 178.9 (C-2). MS (FAB): 471 [(MH)$^+$,100], 443 (54); 427 (10); 288 (14). Anal. Calcd. for $C_{25}H_{18}N_4O_2S_2$: C, 63.81; H, 3.86; N, 11.91. Found C, 63.96; H, 3.78; N, 11.68.

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REFERENCES

1. Brown, D. J., in: Katritzky and Rees *Comprehensive Heterocyclic Chemistry, Vol. 3*; Boulton, A. J.; McKillop, A. Eds.; Pergamon Press: Oxford, 1984; p 57.
2. (a) Baba, M.; Pauwels, R.; Herwig, P.; Clerq, E. D.; Desmyster, J.; Vandepulfe, M. *Biochem. Biophys. Res. Commun.* **1987**, *142*, 128. (b) Clerq, E. D. *J. Med. Chem.* **1986**, *29*, 1561. (c) Clerq, E. D. *Anticancer Res.* **1986**, *6*, 549. (d) Heildelberg, C.; Arafield, F. J. *Cancer Res.* **1963**, *23*, 1226.
3. Dave, C. G.; Shah, P. R.; Dave, K. C.; Patel,V. J. *J. Indian Chem. Soc.* **1989**, *66*, 48.
4. Bousquet, E.; Romero G.; Guerrera, F.; Caruso, A.; Roxas, M. A. *Farmaco Ed. Sci.*, **1985**, *40*, 869. (b) Bousquet, E.; Guerrera, F.; Siracusa, N. A.; Caruso, A.; Roxas, M. A. *Farmaco Ed. Sci.*, **1984**, *39*, 110.
5. (a) Vieweg, H.; Leistner, S.; Wagner, G.; Boehm, N.; Krasset, U.; Grupe, R.; Lohmann D.; Loban, G. East German Patent, **1988**, DD 257,830. *Chem. Abstr.* **1989**, 110, 95262p. (b) Vieweg, H; Leistner, S.; Wagner, G.; Boehm, N.; Krasset, U.; Grupe, R.; Lohmann D.; Loban, G. East German Patent, **1988**, DD 258,234, *Chem. Abstr.* **1989**, 110, 95263q.
6. (a) Leistner, S.; Wagner, G.; Guetscharo, M.; Glusa, E. *Pharmazie*, **1986**, *41*, 54. (b) Radinovskaya, L. A.; Sharamin, A. *Khim. Geterotsikl. Soedin*, **1988**, 805 and references therein. (c) Chaykovsky, M; Lin, M.; Rosowsky, A.; Modest, E. J. *J. Med. Chem.* **1973**, *10*, 188. (d) Eslager, E. F.; Jacob, P. W.; Leslic, M. *J. Heterocyclic Chem.* **1972**, *9*, 775.
7. Madding, G. D.; Thompson, M. D. *J. Heterocyclic Chem.* **1987**, *24*, 581.
8. Cheng, C. C. in *Progress in Medicinal Chemistry*, Vol. 25; Ellis, G. P.; West, G. B. Eds.; Elsevier Science Publishers, Amsterdam, 1989, p. 35.
9. Sishoo, C. J.; Devani, M. B.; Bhadti, V. S. Indian Patent, 1983, 151, 456. *Chem. Abstr.* **1984**, 100, 209858.
10 (a) Peinador, C.; Ojea, V.; Quintela, J. M. *J. Heterocyclic Chem.* **1992**, *29*, 1693. (b) Ojea, V.; Quintela, J. M. *Heterocycles* **1993**, *36*, 1337. (c) Vilar, J.; Quintela, J. M.; Peinador, C.; Veiga, M. C.; Ojea, V. *Heterocycles* **1993**, *36*, 2697.
11. Albert, A.; *Adv. Heterocycl. Chem.* **1982**, *32*, 1.
12. Ellis, G. P. Synthesis of Fused Heterocycles. Heterocyclic Compounds, Vol. 47; Taylor, E. C. Eds.; John Wiley, New York, 1991, pp 210-218.
13. (a) Gusar, N. I. *Russian Chem. Rev.* **1991**, *60*, 146. (b) Golobov, Y. G.; Kasukhin, L. F. *Tetrahedron* **1992**, *48*, 1353.
14. (a) Molina, P.; Fresneda, P. M. *Synthesis* **1989**, 878. (b) Molina, P.; Vilaplana, M. J.; Pérez, J. *Tetrahedron* **1990**, *46*, 7855. (c) Molina, P.; Fresnada, P. M.; Almendros, P. *Tetrahedron* **1991**, *47* 5819. (d) Molina, P.; Aller, E.; Lorenzo, A. *Tetrahedron* **1991**, *47*, 6737. (e) Molina, P.; Vilaplana, M. J.; Pastor, A. *Synthesis* **1992**, 827. (f) Molina, P.; Alajarín, M.; Vidal, A.; Sánchez-Andrada, P. *J. Org. Chem.* **1992**, *57*, 929 and references therein.
15. (a) Saito, T.; Natone, N.; Endo, M.; Yamashita, M.; Ojamada, Y.; Motoki, S. *Chem. Lett.* **1986**, 135.(b) Miyamoto, I.; Matsumoto, J.I.; *Chem. Pharm Bull.* **1988**, *36*, 1321. (c) Wamhoff, H.; Wintersohl, H.; Stolben, S.; Paasch, J.; Nai-jue, Z.; Fang, G. *Liebigs Ann. Chem.* **1990**, 901. (d) Saito, T.; Ohmori, H.; Furuno, E.; Motoki, S. *J.C.S. Chem. Commun.* **1992**, 22.
16. Molina, P.; Arqués, A.; Vinader, M. V. *J. Org. Chem.* **1988**, *53*, 4654.
17. Molina, P.; Alajarín, M.; Arqués, A. *Synthesis* **1982**, 596.

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