An Efficient Synthesis of New Pyrido[4',3':4,5]thieno[2,3-*d*]-pyrimidin-4(3*H*)-one Derivatives

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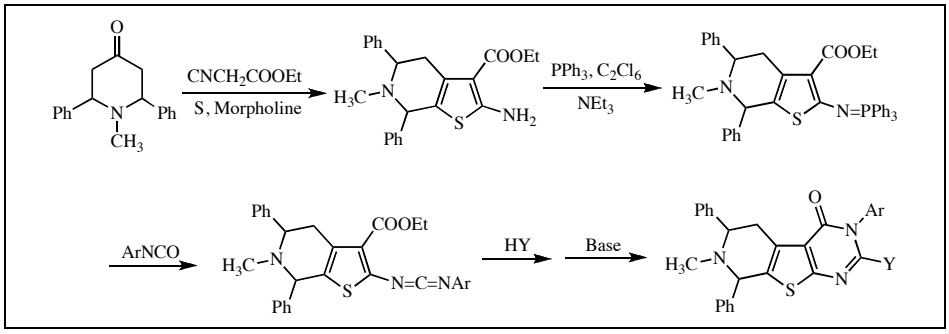

The carbodiimides **5**, obtained from reactions of iminophosphorane **4** with aromatic isocyanates, reacted with amines, phenols or ROH to give 2-substituted 5,6,7,8-tetrahydropyrido[4',3':4,5]thieno[2,3-*d*]-pyrimidin-4(3*H*)-one **7** in the presence of catalytic amount of sodium alkoxide or solid potassium carbonate in satisfactory yields.

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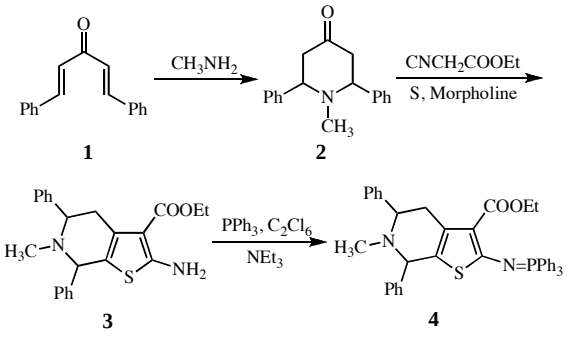
INTRODUCTION

The derivatives of heterocycles containing pyrido-thieno–pyrimidine system possess a broad spectrum of biological activities. They proved to be significant antipyretic [1], anti-inflammatory [2,3] and antiallergic activities [4]. Also some of these compounds show good 5-HT_{1A} agonistical [5] or phosphodiesterase $PDE7_B$ inhibitive activities [6]. The chemistry of pyridothieno-pyrimidinones have also received attention because their starting materials, 2-amino-3-carboxythiophenes, can be conveniently synthesized by Gewald reaction [7]. Synthetically useful approaches to pyridothieno-pyrimidines starting from easily accessible 2-amino-3-carboxythiophenes are therefore of great importance. Recently we have become interested in the preparation of N-heteroaryl iminophosphoranes because these species are promising building blocks for the synthesis of nitrogen heterocycles [8-11]. Herein we wish to report an efficient synthesis of new 2-substituted 5,6,7,8-tetra-hydropyrido[4',3':4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one derivatives via iminophosphorane **4**.

RESULTS AND DISCUSSION

The ethyl 2-amino-4,5,6,7-tetrahydrothieno[2,3-c] pyridine-3-carboxylate **3**, easily obtained by Gewald method from piperidinone **2** [12], ethyl cyanoacetate and sulfur in the presence of morpholine, was converted to iminophosphorane **4** by treatment with triphenyl phosphine, hexachloroethane and triethylamine in dry acetonitrile (Scheme I).

Scheme I



Iminophosphorane **4** reacted with an equimolecular quantity of the aromatic isocyanates to give the carbo-diimides **5**, which were allowed to react with aliphatic amines to provide guanidine intermediates **6** (Y = NR^1R^2). Even in refluxing toluene, the intermediates **6** did not cyclize. However, by treatment with sodium ethoxide in ethanol at room temperature, the intermediates **6** underwent intramolecular heterocyclization to give the expected 2-amino-5,6,7,8-tetrahydropyrido[4',3':4,5]-thieno-[2,3-*d*]pyrimidin-4(3*H*)-ones **7** in satisfactory yields (Scheme II). The results are listed in Table I.

The direct reaction of carbodiimide **5** with phenols did not produce 2-aryloxy 5,6,7,8-tetrahydropyrido-[4',3':4,5]thieno[2,3-d]pyrimidin-4(3*H*)-ones **7** either. However, when carried our in the presence of catalytic amount of potassium carbonate, the reaction took place to give **7** (Y = OAr) in good yields (Table I). The formation

Table I

Physical and Analytical Data of Compounds 7

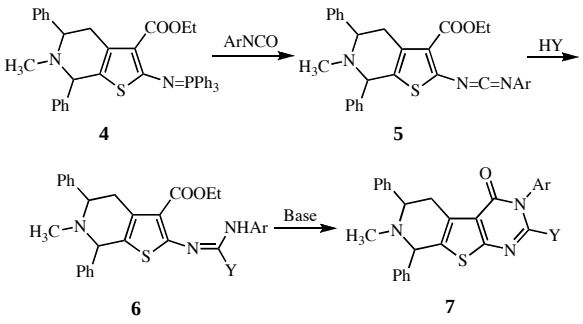
Compd	Ar	Y	Time hours	Mp (°C)	Yield % [a]	Molecular Formula	Analysis % Calcd./Found		
							C	H	N
7a	Ph	$N(n\text{-}C_5H_{11})_2$	8	180-181	75	$C_{38}H_{44}N_4OS$	75.46	7.33	9.26
							75.52	7.23	9.47
7b	Ph	1-pyrrolidinyl	8	299-300	95	$C_{32}H_{30}N_4OS$	74.10	5.83	10.80
							74.08	6.02	10.59
7c	4-ClC_6H_4	$-N(i\text{-}Bu)_2$	8	268-270	92	$C_{36}H_{39}ClN_4OS$	70.74	6.43	9.17
							70.82	6.41	9.25
7d	4-ClC_6H_4	$-N(c\text{-}C_6H_{11})_2$	6	282-283	78	$C_{40}H_{43}ClN_4OS$	72.43	6.53	8.45
							72.20	6.40	8.41
7e	4-FC_6H_4	4-morpholinyl	6	294-296	90	$C_{32}H_{29}FN_4O_2S$	69.54	5.29	10.14
							69.38	5.17	10.26
7f	4-FC_6H_4	$-NEt_2$	8	268-269	91	$C_{32}H_{31}FN_4OS$	71.35	5.80	10.40
							71.58	5.85	10.36
7g	4-FC_6H_4	$N(n\text{-}C_5H_{11})_2$	7	174-175	84	$C_{38}H_{43}FN_4OS$	73.28	6.96	9.00
							73.17	7.12	8.79
7h	4-FC_6H_4	$-N(i\text{-}Bu)_2$	8	234-235	87	$C_{36}H_{39}FN_4O$	72.70	6.61	9.42
							72.76	6.44	9.53
7i	4-FC_6H_4	1-piperidinyl	6	295-296	94	$C_{33}H_{31}FN_4OS$	71.97	5.67	10.17
							72.76	5.84	10.03
7j	Ph	*t*-BuNH	8	269-271	90	$C_{32}H_{32}N_4OS$	73.82	6.19	10.76
							74.07	6.04	10.51
7k	4-ClC_6H_4	*t*-BuNH	8	> 300	86	$C_{32}H_{31}ClN_4OS$	69.24	5.63	10.09
							69.26	5.58	10.12
7l	4-FC_6H_4	*n*-BuNH	6	228-229	88	$C_{32}H_{31}FN_4OS$	71.35	5.80	10.40
							71.52	5.94	10.36
7m	4-FC_6H_4	*t*-BuNH	8	295-296	86	$C_{32}H_{31}FN_4OS$	71.35	5.80	10.40
							71.11	5.62	10.55
7n	Ph	4-ClC_6H_4O	8	279-280	85	$C_{34}H_{26}ClN_3O_2S$	70.88	4.55	7.29
							70.97	4.62	7.06
7o	Ph	4-MeC_6H_4O	5	272-273	82	$C_{35}H_{29}N_3O_2S$	75.65	5.26	7.56
							75.85	5.31	7.48
7p	4-ClC_6H_4	C_6H_5O	6	282-284	80	$C_{34}H_{26}ClN_3O_2S$	70.88	4.55	7.29
							70.75	4.64	7.36
7q	Ph	EtO	6	248-250	95	$C_{30}H_{27}N_3O_2S$	73.00	5.51	8.51
							73.23	5.45	8.38
7r	4-ClC_6H_4	MeO	5	161-162	80	$C_{29}H_{24}ClN_3O_2S$	67.76	4.71	8.17
							67.84	4.82	8.04
7s	4-ClC_6H_4	EtO	6	197-199	88	$C_{30}H_{26}ClN_3O_2S$	68.24	4.96	7.96
							68.52	4.78	7.72
7t	4-FC_6H_4	EtO	6	257-258	85	$C_{30}H_{26}FN_3O_2S$	70.43	5.12	8.21
							70.52	5.32	8.07

[a] Isolated yields based on iminophosphorane **4**.

of **7** can be rationalized in terms of an initial nucleophilic addition of phenoxides to the carbodiimides **5** to give the intermediates **6** which cyclize to give **7**. The direct reaction of carbodiimide **5** with ROH gave a complex mixture, however, when the reaction was carried out in the presence of catalytic amount of RO^-Na^+, the reaction took place smoothly and 2-alkoxy 5,6,7,8-tetrahydro pyrido[4',3':4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-ones **7** (Y = OR) were obtained in satisfactory yields (Table I).

The structure of the synthesized compound **7** was confirmed by their spectral data and elemental analyses. For example the ^1H NMR spectral data of **7a** show signals for $-NCH_2$ at 2.86-2.94 ppm as multiplets, signals of NCH_3 at 1.98 ppm as singlet and signals of $(CH_2)_3CH_3$ at 0.80-1.20 ppm as multiplets. The tetrahydropyridine ring's signals appeared at 4.43 ppm (8-CH) as singlet and 3.10-3.65 ppm (5,6-CH) as multiplets. The phenyl signals

Scheme II



appeared at 7.22-7.53 ppm. The MS spectrum of **7a** shows molecule ion peak (M^+) at m/z 604 with 31% abundance.

In conclusion, we have developed an efficient synthesis of 2-substituted 5,6,7,8-tetrahydropyrido[4',3':4,5]thieno-[2,3-*d*]pyrimidin-4(3*H*)-ones via reaction of functionalized carbodiimides with various amine, phenols or alcohols. Due to the easily accessible and versatile starting material, this method has potential in the synthesis of many biologically and pharmaceutically active pyridothienopyrimidinone derivatives.

EXPERIMENTAL

Melting points were determined using a X-4 model apparatus and are uncorrected. MS were measured on a Finnigan Trace MS spectrometer. NMR spectra were recorded in $CDCl_3$ on a Varian Mercury Plus 400 (400 MHz) spectrometer and chemical shifts (δ) were given in ppm using $(CH_3)_4Si$ as an internal reference (δ = 0). IR spectra were recorded on a PE-983 infrared spectrometer as KBr pellets with absorption in cm^{-1}. UV spectra were recorded on a SCINCO UV S-3100 spectrometer. Elementary analyses were taken on a Vario EL III elementary analysis instrument.

Ethyl 2-amino-5,7-diphenyl-6-methyl-4,5,6,7-tetrahydro-thieno[2,3-*c*]pyridine-3-carboxylate (**3**). To a stirred mixture of 1.33 g (0.005 mole) of piperidinone (**2**) [12], 0.16 g (0.005 mole) of sulfur, 0.57 g (0.005 mole) of ethyl cyanoacetate in 20 mL of ethanol, was added 1.2 mL of morpholine. After the mixture was stirred at 35 °C for 48 hours, the solid was collected by filtration and recrystallized from ethanol to give **3** as light yellow needles, 1.25 g (64%), mp 195-197°; ^{1}H NMR ($CDCl_3$): δ 1.22 (t, J = 7.2 Hz, 3H), 1.89 (s, 3H), 2.98-3.57 (m, 3H), 4.20 (q, J = 7.2 Hz, 3H), 4.25 (s, 1H), 5.88 (s, 2H), 7.25-7.47 (m, 10H); MS: m/z (%) 392 (48, M^+), 315 (50), 269 (30), 198 (18), 118 (100), 91 (30). *Anal*. Calcd. for $C_{23}H_{24}N_2O_2S$: C, 70.38; H, 6.16; N, 7.14. Found: C, 70.15; H, 6.23; N, 7.35.

Ethyl 5,7-diphenyl-6-methyl-2-(triphenylphosphoranylidene)amino-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate (**4**). To a mixture of ethyl 2-amino-5,7-diphenyl-6-methyl-4,5,6,7-tetrahydro-thieno[2,3-*c*]pyridine-3-carboxylate (**3**) (3.14 g, 8 mmol), PPh_3 (3.14 g, 12 mmol) and C_2Cl_6 (2.84 g, 12 mmol) in dry CH_3CN (40 mL), was added dropwise NEt_3 (2.42 g, 24 mmol) at room temperature. The color of the reaction mixture quickly turned yellow. After stirring for 4 h, the solvent was removed under reduced pressure and the residue was recrystallized from EtOH to give iminophosphorane **4** as light yellow needles, 4.33 g (83%), mp 218-219°; ^{1}H NMR ($CDCl_3$): δ 1.24 (t, J = 7.2 Hz, 3H), 1.85 (s, 3H), 3.02-3.54 (m, 3H), 4.16 (q, J = 7.2 Hz, 3H), 4.23 (s, 1H), 7.19-7.75 (m, 25H); MS: m/z (%) 652 (48, M^+), 606 (63), 487 (100), 436 (23), 316 (10), 274 (23). *Anal*. Calcd. for $C_{41}H_{37}N_2O_2PS$: C, 75.44; H, 5.71; N, 4.29. Found: C, 75.68; H, 5.58; N, 4.32.

General Preparation of 2-Amino-5,6,7,8-tetrahydro pyrido[4',3':4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-ones (7a-7m). To a solution of iminophosphorane **4** (1.30 g, 2 mmol) in anhydrous CH_2Cl_2 (10 mL) was added aromatic isocyanate (2 mmol) under nitrogen atmosphere at room temperature. After the reaction mixture was left unstirred for 6-12 h at 0-5 °C, the iminophosphorane **4** had disappeared (TLC monitored). The solvent was removed under reduced pressure and Et_2O/ petroleum ether (1:2, 20 mL) was added to precipitate triphenylphosphine oxide. Removal of the solvent gave carbodiimides **5**, which were used directly without further purification. To the solution of **5** in dichloromethane (10 mL) was added aliphatic amine (2 mmol). After the reaction mixture was left unstirred for 5-6 h, the solvent was removed and anhydrous EtOH (10 mL) with several drops of EtONa in EtOH was added. The mixture was stirred for 6-8 h at room temperature. The solution was condensed and residue was recrystallized from EtOH to give the expected cyclic compounds **7a**-**7m** in good yields.

2-Di(*n*-pentyl)amino-7-methyl-3,6,8-triphenyl-5,6,7,8-tetra hydropyrido[4',3':4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (7a). ^{1}H NMR ($CDCl_3$): δ 0.80-1.20 (m, 18H), 1.98 (s, 3H), 2.86-2.94 (m, 4H), 3.10-3.65 (m, 3H), 4.43 (s, 1H), 7.22-7.53 (m, 15H); ir (potassium bromide): 1680 (C=O), 1542, 1376, 1214 cm^{-1}; uv: λ max 302 nm; MS: m/z (%) 604 (31, M^+), 484 (42), 359 (100), 318 (32), 274 (52), 218 (10).

7-Methyl-2-(1-pyrrolidinyl)-3,6,8-triphenyl-5,6,7,8-tetra-hydropyrido[4',3':4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (7b). ^{1}H NMR ($CDCl_3$): δ 1.62-1.67 (m, 4H), 1.97 (s, 3H), 2.96 (t, J = 6.4 Hz, 4H), 3.08-3.66 (m, 3H), 4.45 (s, 1H), 7.19-7.51 (m, 15H); ir (potassium bromide): 1684 (C=O), 1545, 1368, 1210 cm^{-1}; uv: λ max 302 nm; MS: m/z (%) 518 (11, M^+), 484 (9), 374 (18), 359 (100), 318 (11), 274 (12).

3-(4-Chlorophenyl)-2-di(*i*-butyl)amino-6,8-diphenyl-7-methyl-5,6,7,8-tetrahydropyrido[4',3':4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (7c). ^{1}H NMR ($CDCl_3$): δ 0.74 (d, J = 6.4 Hz, 12H), 1.72-1.79 (m, 2H), 1.97 (s, 3H), 2.72-1.84 (m, 4H), 3.11-3.64 (m, 3H), 4.45 (s, 1H), 7.17-7.53 (m, 14H); ir (potassium bromide): 1685 (C=O), 1544, 1378, 1214 cm^{-1}; uv: λ max 300 nm; MS: m/z (%) 611 (13, M^+), 534 (77), 490 (68), 389 (14), 207 (28), 118 (100).

3-(4-Chlorophenyl)-2-dicyclohexylamino-6,8-diphenyl-7-methyl-5,6,7,8-tetrahydropyrido[4',3':4,5]thieno[2,3-*d*]-pyrimidin-4(3*H*)-one (7d). ^{1}H NMR ($CDCl_3$): δ 1.00-1.67 (m, 20H), 1.97 (s, 3H), 2.93 (t, J = 11.2 Hz, 2H), 3.12-3.64 (m, 3H), 4.45 (s, 1H), 7.15-7.53 (m, 14H); ir (potassium bromide): 1688 (C=O), 1540, 1385, 1226 cm^{-1}; uv: λ max 300 nm; MS: m/z (%) 663 (99, M^+), 586 (100), 543 (94), 460 (22), 377 (26), 118 (88).

6,8-Diphenyl-3-(4-fluorophenyl)-7-methyl-2-(4-morpholinyl)-5,6,7,8-tetrahydropyrido[4',3':4,5]thieno[2,3-*d*]-pyrimidin-4(3*H*)-one (7e). ^{1}H NMR ($CDCl_3$): δ 1.97 (s, 3H), 3.03 (t, J = 4.0 Hz, 4H), 3.11-3.66 (m, 7H), 4.47 (s, 1H), 7.13-7.51 (m, 14H); ^{13}C NMR ($CDCl_3$): δ 164.5, 162.7, 161.1, 159.3, 154.2, 143.9, 143.5, 134.2, 132.5, 130.4, 130.3, 129.4, 128.7, 128.4, 128.2, 128.0, 127.7, 127.2, 116.8, 115.9, 115.8, 69.3, 66.6, 65.9, 49.2, 41.3, 35.9; ir (potassium bromide): 1688 (C=O), 1528, 1444, 1220 cm^{-1}; uv: λ max 304 nm; MS: m/z (%) 552 (67, M^+), 475 (100), 432 (68), 207 (20), 118 (54), 95 (14).

2-Diethylamino-6,8-diphenyl-3-(4-fluorophenyl)-7-methyl-5,6,7,8-tetrahydropyrido[4',3':4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (7f). ^{1}H NMR ($CDCl_3$): δ 0.80 (t, J = 7.2 Hz, 6H), 1.98 (s, 3H), 2.94-3.04 (m, 4H), 3.09-3.65 (m, 3H), 4.46 (s, 1H), 7.11-7.52 (m, 14H); ^{13}C NMR ($CDCl_3$): δ 165.3, 162.8, 161.2, 159.9, 154.6, 144.0, 143.6, 133.4, 133.0, 131.3, 129.9, 129.4, 129.3, 129.0, 128.6, 127.9, 127.6, 116.7, 116.5, 115.8, 115.1, 114.9, 69.8, 68.7, 46.4, 45.1, 43.7, 13.1; ir (potassium bromide): 1686 (C=O), 1525, 1508, 1381, 1226 cm^{-1}; uv: λ max 304 nm; MS: m/z (%) 538 (36, M^+), 461 (57), 418 (42), 208 (8), 193 (23), 118 (100).

2-Dipentylamino-6,8-diphenyl-3-(4-fluorophenyl)-7-methyl-5,6,7,8-tetrahydropyrido[4',3':4,5]thieno[2,3-*d*]-pyrimidin-4(3*H*)-one (7g). ^{1}H NMR ($CDCl_3$): δ 0.83 (t, J = 7.2 Hz, 6H), 1.00-1.22 (m, 12H), 1.97 (s, 3H), 2.86-2.97 (m, 4H), 3.12-3.65 (m, 3H), 4.46 (s, 1H), 7.11-7.52 (m, 14H); ^{13}C NMR ($CDCl_3$): δ 165.4, 163.1, 161.5, 159.9, 154.7, 143.9, 143.6, 133.4, 132.8, 131.2, 129.8, 129.3, 129.1, 129.0, 128.5, 127.9, 127.6, 127.4, 126.9, 126.4, 116.6, 116.4, 115.6, 115.0, 114.8, 69.8, 68.7, 52.4, 51.1, 49.8, 29.1, 27.0, 22.3, 14.6; ir (potassium bromide): 1685 (C=O), 1526, 1384, 1234 cm^{-1}; uv: λ max 303 nm; MS: m/z (%) 623 (99, M^++1), 546 (92), 503 (100), 345 (22), 208 (41), 118 (95).

2-Di(*i*-butyl)amino-6,8-diphenyl-3-(4-fluorophenyl)-7-methyl-5,6,7,8-tetrahydropyrido[4',3':4,5]thieno[2,3-*d*]-pyrimidin-4(3*H*)-one (7h). ^{1}H NMR ($CDCl_3$): δ 0.74 (d, J = 6.4 Hz, 12H), 1.72-1.77 (m, 2H), 1.98 (s, 3H), 2.74-2.82 (m, 4H), 3.10-3.64 (m, 3H), 4.46 (s, 1H), 7.12-7.53 (m, 14H); ir (potassium bromide): 1686 (C=O), 1528, 1379, 1230 cm^{-1}; uv: λ max 302 nm; MS: m/z (%) 594 (94, M^+), 518 (100), 474 (68), 208 (13), 118 (62), 91 (10).

6,8-Diphenyl-3-(4-fluorophenyl)-7-methyl-2-(1-piperidinyl)-5,6,7,8-tetrahydropyrido[4',3':4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (7i). ^{1}H NMR ($CDCl_3$): δ 0.74 (d, J = 6.4 Hz, 12H), 1.72-1.77 (m, 2H), 1.98 (s, 3H), 2.74-2.82 (m, 4H), 3.10-3.64 (m, 3H), 4.46 (s, 1H), 7.12-7.53 (m, 14H); ir (potassium bromide): 1686 (C=O), 1524, 1382, 1225 cm^{-1}; uv: λ max 304 nm; MS: m/z (%) 550 (64, M^+), 473 (97), 430 (71), 205 (31), 149 (24), 118 (100).

2-(*t*-Butyl)amino-7-methyl-3,6,8-triphenyl-5,6,7,8-tetrahydropyrido[4',3':4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (7j). ^{1}H NMR ($CDCl_3$): δ 1.27 (s, 9H), 1.97 (s, 3H), 3.11-3.65 (m, 3H), 3.93 (s, 1H), 4.44 (s, 1H), 7.18-7.56 (m, 15H); ^{13}C NMR ($CDCl_3$): δ 166.7, 159.0, 149.3, 144.3, 143.8, 134.8, 130.4, 130.2, 129.6, 129.1, 128.8, 128.7, 128.6, 128.3, 128.2, 127.9, 127.8, 127.1, 113.7, 69.3, 66.8, 52.6, 41.4, 36.0, 28.8; ir (potassium bromide): 3430 (NH), 1678 (C=O), 1553, 1335, 1211 cm^{-1}; uv: λ max 301 nm; MS: m/z (%) 520 (98, M^+), 444 (97), 401 (100), 387 (44), 224 (36), 118 (99).

2-(*t*-Butyl)amino-3-(4-chlorophenyl)-6,8-diphenyl-7-methyl-5,6,7,8-tetrahydropyrido[4',3':4,5]thieno[2,3-*d*]-pyrimidin-4(3*H*)-one (7k). ^{1}H NMR ($CDCl_3$): δ 1.27 (s, 9H), 1.97 (s, 3H), 3.14-3.65 (m, 3H), 3.87 (s, 1H), 4.44 (s, 1H), 7.13-7.53 (m, 14H); ir (potassium bromide): 3433 (NH), 1680 (C=O), 1554, 1335, 1220 cm^{-1}; uv: λ max 300 nm; MS: m/z (%) 555 (27, M^+), 477 (53), 434 (35), 378 (45), 118 (100), 91 (62).

2-(*n*-Butyl)amino-3-(4-fluorophenyl)-6,8-diphenyl-7-methyl-5,6,7,8-tetrahydropyrido[4',3':4,5]thieno[2,3-*d*]-pyrimidin-4(3*H*)-one (7l). ^{1}H NMR ($CDCl_3$): δ 0.85 (t, J = 7.2 Hz, 3H), 1.18-1.43 (m, 4H), 1.97 (s, 3H), 3.23-3.66 (m, 5H), 3.98 (t, J = 4.2 Hz, 1H), 4.45 (s, 1H), 7.20-7.52 (m, 14H); ^{13}C NMR ($CDCl_3$): δ 167.2, 164.2, 161.4, 158.8, 150.3, 144.1, 143.7, 130.8, 130.5, 130.2, 129.0, 128.6, 128.3, 128.2, 127.8, 127.7, 127.1, 117.7, 117.4, 113.6, 69.2, 66.7, 41.6, 41.3, 35.9, 31.1, 19.9, 13.7; ir (potassium bromide): 3438 (NH), 1683 (C=O), 1552, 1334, 1222 cm^{-1}; uv: λ max 300 nm; MS: m/z (%) 538 (51, M^+), 461 (84), 418 (83), 118 (100), 91 (43), 77 (40).

2-(*t*-Butyl)amino-3-(4-fluorophenyl)-6,8-diphenyl-7-methyl-5,6,7,8-tetrahydropyrido[4',3':4,5]thieno[2,3-*d*]-pyrimidin-4(3*H*)-one (7m). ^{1}H NMR ($CDCl_3$): δ 1.28 (s, 9H), 1.97 (s, 3H), 3.08-3.65 (m, 3H), 3.89 (s, 1H), 4.44 (s, 1H), 7.17-7.53 (m, 14H); ^{13}C NMR ($CDCl_3$): δ 166.6, 164.3, 161.6, 159.0, 149.1, 144.2, 143.7, 131.6, 130.5, 130.0, 129.3, 129.0, 128.6, 127.9, 127.6, 127.5, 127.1, 118.3, 116.7, 113.6, 69.8, 68.7, 52.7, 45.2, 40.9, 28.8; ir (potassium bromide): 3437 (NH), 1681 (C=O), 1554, 1336, 1225 cm^{-1}; uv: λ max 301 nm; MS: m/z (%) 538 (5, M^+), 461 (5), 419 (11), 118 (100), 91 (26), 57 (97).

General Preparation of 2-Aryloxy-5,6,7,8-tetrahydro pyrido[4',3':4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-ones (7n-7p). To the solution of carbodiimides **5** prepared above in dry acetonitrile (10 mL) was added substituted phenol (2 mmol) and solid K_2CO_3 (0.014 g, 0.1 mmol). The mixture was stirred for 5-8 h at room temperature and filtered. The filtrate was condensed and the residual was recrystallized from EtOH to give **7n**-**7p** in good yields.

2-(4-Chlorophenoxy)-7-methyl-3,6,8-triphenyl-5,6,7,8-tetrahydropyrido[4',3':4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (7n). ^{1}H NMR ($CDCl_3$): δ 1.97 (s, 3H), 3.17-3.67 (m, 3H), 4.46 (s, 1H), 6.98-7.53 (m, 19H); ir (potassium bromide): 1692 (C=O), 1556, 1486, 1258 cm^{-1}; uv: λ max 301 nm; MS: m/z (%) 575 (16, M^+), 498 (43), 456 (100), 118 (96), 91 (27), 77 (70).

7-Methyl-2-(4-methylphenoxy)-3,6,8-triphenyl-5,6,7,8-tetrahydropyrido[4',3':4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (7o). ^{1}H NMR ($CDCl_3$): δ 1.97 (s, 3H), 2.31 (s, 3H), 3.18-3.67 (m, 3H), 4.46 (s, 1H), 6.90-7.50 (m, 19H); ^{13}C NMR ($CDCl_3$): δ 163.3, 158.9, 152.7, 149.4, 143.8, 143.4, 135.6, 134.6, 129.8, 129.3, 128.9, 128.6, 128.4, 128.1, 127.7, 127.2, 121.0, 117.4, 69.2, 66.6, 49.3, 41.3, 20.8; ir (potassium bromide): 1694 (C=O), 1556, 1495, 1257 cm^{-1}; uv: λ max 300 nm; MS: m/z (%) 555 (99, M^+), 479 (98), 435 (100), 315 (51), 118 (99), 91 (88).

3-(4-Chlorophenyl)-2-phenoxy-6,8-diphenyl-7-methyl-5,6,7,8-tetrahydropyrido[4',3':4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (7p). ^{1}H NMR ($CDCl_3$): δ 1.97 (s, 3H), 3.18-3.67 (m, 3H), 4.46 (s, 1H), 7.02-7.48 (m, 14H); ^{13}C NMR ($CDCl_3$): δ 163.2, 158.6, 152.2, 151.4, 143.7, 143.3, 134.9, 133.1, 130.4, 129.6, 129.4, 129.2, 128.7, 128.5, 128.1, 127.8, 127.3, 126.1, 121.2, 117.4, 69.1, 66.6, 41.3, 35.6; ir (potassium bromide): 1692 (C=O), 1555, 1488, 1260 cm^{-1}; uv: λ max 302 nm; MS: m/z (%) 575 (17, M^+), 500 (21), 455 (37), 117 (100), 91 (23), 76 (50).

General Preparation of 2-Alkoxy-5,6,7,8-tetrahydro pyrido-[4',3':4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-ones (7q-7t). To the solution of carbodiimides **5** prepared above in ROH (10 mL) was added several drops of RONa in ROH. The mixture was stirred for 5-6 h at room temperature. The solution was condensed and the residual was recrystallized from EtOH to give **7q-7t**.

2-Ethoxy-7-methyl-3,6,8-triphenyl-5,6,7,8-tetrahydro-pyrido[4',3':4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (7q). ^{1}H NMR ($CDCl_3$): δ 1.18 (t, J = 7.2 Hz, 3H), 1.98 (s, 3H), 3.13-3.67 (m, 3H), 4.33 (q, J = 7.2 Hz, 2H), 4.48 (s, 1H), 7.16-7.52 (m, 15H); MS: m/z (%) 493 (46, M^+), 416 (100), 374 (67), 345 (38), 118 (74), 91 (27).

3-(4-Chlorophenyl)-6,8-diphenyl-2-methoxy-7-methyl-5,6,7,8-tetrahydropyrido[4',3':4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (7r). ^{1}H NMR ($CDCl_3$): δ 1.97 (s, 3H), 3.12-3.67 (m, 3H), 3.86 (s, 3H), 4.48 (s, 1H), 7.11-7.51 (m, 14H); ^{13}C NMR ($CDCl_3$): δ 163.8, 158.6, 153.2, 143.8, 143.4, 134.6, 133.8, 133.0, 129.6, 129.4, 129.3, 128.7, 128.4, 128.2, 128.0, 127.7, 127.2, 116.7, 69.2, 66.6, 56.0, 41.3, 35.6; ir (potassium bromide): 1695 (C=O), 1561, 1492, 1263 cm^{-1}; uv: λ max 304 nm; MS: m/z (%) 513 (41, M^+), 436 (100), 393 (98), 153 (33), 118 (59), 91 (22).

3-(4-Chlorophenyl)-6,8-diphenyl-2-ethoxy-7-methyl-5,6,7,8-tetrahydropyrido[4',3':4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (7s). ^{1}H NMR ($CDCl_3$): δ 1.21 (t, J = 7.2 Hz, 3H), 1.97 (s, 3H), 3.13-3.66 (m, 3H), 4.32 (q, J = 7.2 Hz, 2H), 4.47 (s, 1H), 7.10-7.52 (m, 14H);); ^{13}C NMR ($CDCl_3$): δ 164.0, 158.8, 152.7, 143.9, 143.4, 134.5, 133.6, 133.2, 129.6, 129.3, 128.7, 128.4, 128.2, 128.0, 127.8, 127.2, 116.6, 69.2, 66.6, 65.2, 41.3,

35.7, 14.0; ir (potassium bromide): 1691 (C=O), 1557, 1491, 1261 cm^{-1}; uv: λ max 300 nm; MS: m/z (%) 527 (9, M^+), 450 (33), 408 (21), 171 (25), 153 (33), 118 (100).

6,8-Diphenyl-2-ethoxy-3-(4-fluorophenyl)-7-methyl-5,6,7,8-tetrahydropyrido[4',3':4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (7t). ^1H NMR ($CDCl_3$): δ 1.19 (t, J = 7.2 Hz, 3H), 1.98 (s, 3H), 3.17-3.66 (m, 3H), 4.33 (q, J = 7.2 Hz, 2H), 4.48 (s, 1H), 7.13-7.52 (m, 14H);); ir (potassium bromide): 1698 (C=O), 1560, 1492, 1264 cm^{-1}; uv: λ max 300 nm; MS: m/z (%) 511 (50, M^+), 434 (100), 393 (51), 363 (42), 118 (8), 91 (10).

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