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Synthesis of pyrido and pyrazinodithienodipyrimidine-4,8(3*H*,9*H*)-dione derivatives by the aza-Wittig methodology

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Abstract—A one-pot synthesis of the hitherto unreported pyrido[5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione **6a**–**o** and pyrazino[5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione **6p**–**y** pentaheterocyclic systems, based on the tandem aza-Wittig heterocumulene-mediated annulation strategy is described.

1. Introduction

Synthetic heterocycles have widespread interest as herbicides, insecticides, dyes, organic-conductors, and drugs. Nitrogen-containing heterocycles are of broad pharmaceutical interest and this justifies continuing efforts in the development of structure-activity relationship in this series and of new synthetic strategies.[1] There is a enormous interest in the synthesis of new heterocyclic rings stimulated by recent reports that showed antitumor activity in a wide range of polyheterocyclic compounds isolated from marine organisms.[2] Compounds containing a fused pyrimidine ring have significant biological activity, particularly in cancer and virus research.[3] Among these heterocycles, thienopyrimidine derivatives are an important class of heterocyclic compounds in pharmaceutical discovery research. Anti-allergic,[4] antianaphilactic,[5] anti-inflammatory,[6] analgesic and antipyretic,[7] and antineoplasic[8] activities have been described for these compounds.

The aza-Wittig reaction has become one of the most important synthetic methods for constructing novel C═N, N═N, and S═N double bonds containing compounds, especially in modern nitrogen heterocyclic synthesis. In recent years, there has been a significant interest in the chemistry of iminophosphoranes (λ5-phosphazenes, phosphine imines) because of their utility for the construction of nitrogen-containing heterocycles compounds, and many interesting heterocyclization reactions involved functionalized iminophosphoranes have been reviewed.[9] These compounds can react with carbonyl compounds to form imines, and with isocyanates, isothiocyanates, carbon dioxide and carbon disulfide, giving rise to the corresponding heterocumulenes.[10] Aza-Wittig reactions can be divided into an intramolecular and an intermolecular variant. The intramolecular aza-Wittig reaction is a powerful tool reaction for the synthesis of 5–7 membered ring heterocycles[11] and the intermolecular aza-Wittig reaction followed by electrocyclization, intramolecular cycloaddition or heterocyclization, has been utilized for the synthesis of many important nitrogen heterocycles,[12] and, on the other hand, the utilization of the aza-Wittig reaction in the synthesis of biologically important heterocyclic natural products has been recently reviewed.[13]

Iminophosphoranes derived from *N*-aminoheterocycles are valuable precursors for the preparation of fused heterocycles which may be neutral, cationic or mesoionic.[14] Recently, we have reported the synthesis of fused pyrimidines based on the tandem aza-Wittig heterocumulene-mediated annulation strategy.[15]

2. Results and discussion

Work in our laboratories has been recently concerned with the discovery and development of synthesis of new heterocycles systems containing thienopyrimidine moiety in order to search for new pharmacological or biologically active compounds. We have previously reported on the synthesis of novel tri- and tetracyclic ring systems, containing the thienopyrimidine skeleton, with antiinflammatory and antihistaminic activity.[16] We now describe here, as a further extension of the aza-Wittig-type methodology the synthesis of the hitherto unreported pyrido

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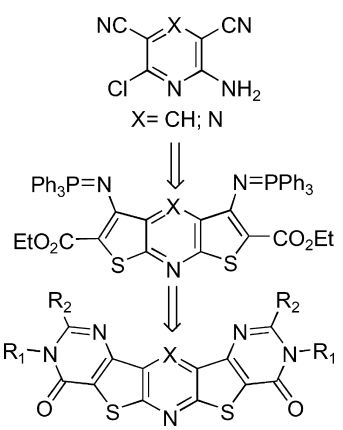
[5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione **6a**–**o** and pyrido[5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione **6p**–**y**, utilizing for the first time 2,6-dichloropyridine-3,5-dicarbonitrile **1a** and 3,5-dichloropyrazine-2,6-dicarbonitrile **1b** as the starting materials. The strategy used for the development of these compounds was focused as shown in Scheme 1. The bis *N*-heteroaryliminophosphoranes **3a**,**b** appear to serve as a good building block for these heterocycles. They can be synthesized from 2,6-dichloropyridine-3,5-dicarbonitrile and 2,6-dichloropyrazine-3,5-dicarbonitrile, respectively.

Pentaheterocyclic compounds **6a**–**o** and **6p**–**y** were obtained in a one-pot reaction of the corresponding iminophosphoranes of heteroaromatic β-enamino esters **3a** and **3b** with isocyanates, followed by heterocyclization on addition of amines.

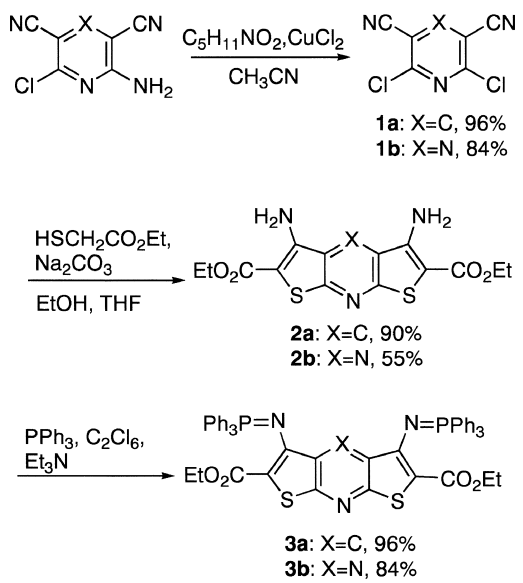
The starting compounds for the aza-Wittig reaction heterocyclization sequence were prepared from the readily available heterocyclic β-enaminoesters **2a**–**b**. First, 2,6-dichloropyridine-3,5-dicarbonitrile **1a** and 2,6-dichloropyrazine-3,5-dicarbonitrile **1b** were formed by nitrosation reaction of the corresponding 2-aminoderivatives[17] following a previously described procedure.[18] The thiophene rings were added on the pyridine and pyrazine rings by condensing **1a**–**b** with ethyl 2-mercaptoacetate in the presence of an equimolecular amount of potassium carbonate in refluxing ethanol to give ethyl 3,5-diamino-dithieno[3′,2′-*e*:2,3-*b*]pyridine-2,6-dicarboxylate **2a** and ethyl 3,5-diamino-dithieno[3′,2′-*e*:2,3-*b*]pyrazine-2,6-dicarboxylate **2b** in good yields.

The key iminophosphoranes **3a**–**b** were obtained by a modified Kirsanov reaction of the β-enamino esters **2a**–**b** with in situ prepared dichlorotriphenylphosphorane using a hexachloroethane-triphenylphosphine-triethylamine reagent system (Scheme 2).[19] The molecular structure of the iminophposphoranes were supported by the general data (IR, ^{1}H NMR, ^{13}C NMR, ^{31}P NMR, and mass spectra) and elemental analysis.

Aza-Wittig reaction of bisimonophosphoranes **3a**–**b** with arylisocyanates, followed by heterocyclization on addition of secondary amines directly affords substituted pyrido[5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]di-pyrimidine-4,8(3*H*,9*H*)-dione **6a**–**o** and pyrazino [5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione **6p**–**y**. Reaction of bis-imino-phosphoranes with arylisocyanates and secondary amines at room temperature resulted in the formation of the corresponding guanidine-type intermediate derivatives **5a**–**f**, the key intermediates for the processes, that could be isolated in the above mentioned conditions. Pyrimido-annulation occurs via a heterocumulene moiety, available from the reaction of the *N*-heteroaryliminophosphorane and the isocyanate as highly reactive intermediates.



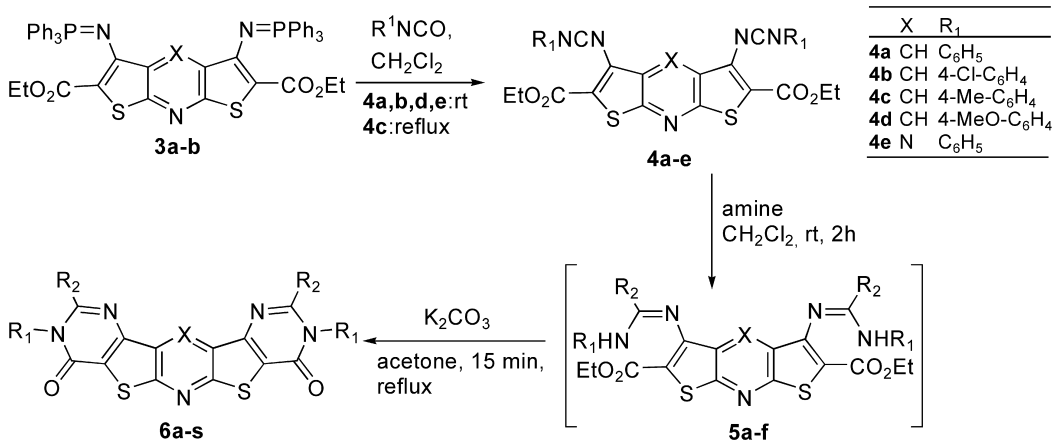
Scheme 1.



Scheme 2.

Those carbodiimide derivatives **4a**–**e** have been isolated by treatment of bis-triphenyliminophosphoranes **3a**–**b** with aryl isocyanates in dry CH_2Cl_2 at room temperature. Addition of a secondary amine to the highly reactive cumulenic system followed by intramolecular heteroconjugate addition annulation gives the final penta- and hexaaza-indenefluorenediones **6a**–**o** and **6p**–**y**. Direct cyclization of the initially formed carbodiimide via 1,3-OEt migration followed by electrocyclization (Wamhoff's pyrimidoannelation)[20] was not observed in this case. In the presence of anhydrous sodium carbonate, the separated guanidine-type intermediate derivatives **5a**–**f** underwent intramolecular heterocyclization across the electrophilic ester functionality to give the fused heterocyclic compounds **6a**–**o** and **6p**–**y** (Scheme 3).

The structures of carbodiimide compounds **4a**–**e**, guanidine compounds **5a**–**f**, and fused pyrimidines **6a**–**o** and **6p**–**y** were confirmed by their elemental analyses and spectroscopic data. The mass spectra showed the expected molecular ion peak and the IR spectra of guanidine-type intermediates **5a**–**f** showed a strong absorption at ν=3320–3373 cm^{-1} attributed to the NH group, while in the ^{1}H NMR spectra, the NH proton appear at δ=5.77–6.92 ppm as a singlet, in addition to the set of signals due to the ethoxy group. Also, the ^{13}C NMR spectra showed signals between δ=14.28–14.49 and 60.5–66.4 ppm due to ethoxy groups.



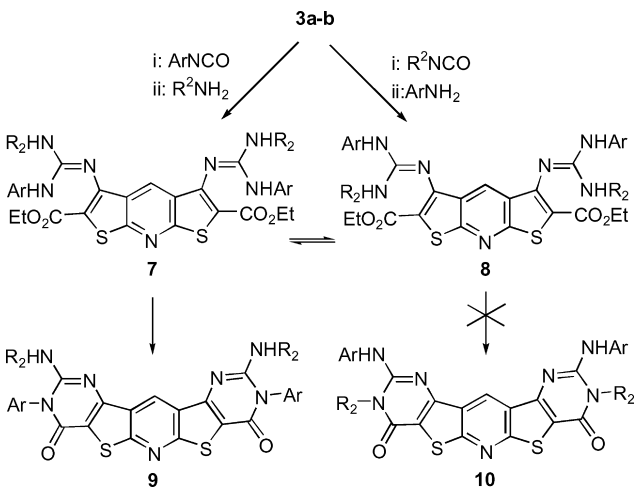
	X	R^1
4a	CH	C_6H_5
4b	CH	4-Cl-C_6H_4
4c	CH	4-Me-C_6H_4
4d	CH	4-MeO-C_6H_4
4e	N	C_6H_5

	X	R^1	R^2		X	R^1	R^2		X	R^1	R^2
5a	CH	C_6H_5	Thiomorpholino	**6f**	CH	4-Cl-C_6H_4	Piperidino	**6q**	N	C_6H_5	Morpholino
5b	CH	C_6H_5	Diethylamino	**6g**	CH	4-Me-C_6H_4	Morpholino	**6r**	N	C_6H_5	Piperidino
5c	CH	C_6H_5	Morpholino	**6h**	CH	4-Me-C_6H_4	Piperidino	**6s**	N	C_6H_5	Isopropylamino
5d	CH	4-MeO-C_6H_4	Morpholino	**6i**	CH	4-MeO-C_6H_4	Morpholino	**6t**	N	4-Cl-C_6H_4	Morpholino
5e	CH	4-Cl-C_6H_4	Piperidino	**6j**	CH	4-MeO-C_6H_4	Pyperidino	**6u**	N	4-Cl-C_6H_4	Piperidino
5f	CH	C_6H_5	Isopropylamino	**6k**	CH	C_6H_5	*n*-Butylamino	**6v**	N	4-Me-C_6H_4	Morpholino
6a	CH	C_6H_5	Diethylamino	**6l**	CH	C_6H_5	Isopropylamino	**6w**	N	4-Me-C_6H_4	Piperidino
6b	CH	C_6H_5	Thiomorpholino	**6m**	CH	4-Cl-C_6H_4	Isopropylamino	**6x**	N	4-MeO-C_6H_4	Morpholino
6c	CH	C_6H_5	Morpholino	**6n**	CH	4-Me-C_6H_4	Isopropylamino	**6y**	N	4-MeO-C_6H_4	Piperidino
6d	CH	C_6H_5	Piperidino	**6o**	CH	4-MeO-C_6H_4	Isopropylamino				
6e	CH	4-Cl-C_6H_4	Morpholino	**6p**	N	C_6H_5	Thiomorpholino				

Scheme 3.

After heterocyclization, the spectra of compounds **6a**–**o** and **6p**–**y** did not include those type of signals.

Two isomeric pyrimidothieno derivatives, **9** and **10**, may be produced in the treatment of bis-*N*-heteroarylimino-phosphoranes **3a**–**b** with ArNCO/R^2NH_2 or R^2NCO/$ArNH_2$ via guanidine-type intermediates **7** and **8** (Scheme 4), but these reactions afforded only **9**, compound **10** not being formed. In addition, only pentacyclic compound **9** was obtained by the reaction of carbodiimide **4a**–**e** with primary amines (the guanidine intermediate **5f** was isolated). These selectivity results can probably be explained by the large difference in cyclization rates due the steric hindrance around the Ph and



Scheme 4.

isopropyl or butyl groups.[21] Mass and spectroscopic data are in good agreement with the proposed structures. The FAB-mass spectra show the expected molecular ion peaks and the fragmentation pattern is in accord with the proposed structures. In particular, in the ^{1}H NMR spectra, the NH-isopropyl groups of compounds **6l**–**o** and **6 s** appear characteristically as broad doublets at δ=4.05–6.29 ppm. In addition, the NH-butyl proton in compound **6k** resonates as a triplet confirming the proposed structures.

In conclusion, the present study demonstrates that the tandem aza-Wittig-heterocumulene-mediated annulation strategy affords a facile, efficient and general one-pot route to previously unreported pentacyclic dipyrimidodithienopyridine **6a**–**o** and dipyrimidodithienopyrazine **6p**–**y** systems bearing various substituents on the pyrimidine ring. Pentaheterocyclic compounds **6a**–**o** and **6p**–**y** can be useful compounds in medicinal chemistry since the pyrimido and thiophene moieties display a broad range of biological activities and have been widely used as pharmaceuticals.

3. Experimental

All reagents used were comercial grade chemicals from freshly opened containers. Melting points were determinated on a Bibby SMP3 apparatus and are uncorrected. IR spectra were recorded as potassium bromide disks on a Bruker vector 22 FT-IR. ^{1}H and ^{13}C NMR spectra were obtained on a Bruker AC 200F instrument at room temperature. Mass spectra were obtained on a VG-QUATTRO spectrometer. The Silica gel 60F-254 used for analytical thin layer chromatography were

purchased from Merck. Microanalyses for C, H, N, and S were performed by the elemental analyses general services of the University of La Coruña.

3.1. Synthesis of 2,6-dichloropyridine-3,5-dicarbonitrile (1a) and 3,5-dichloro-pyrazine-2,6-dicarbonitrile (1b)

To a solution of 2-amino-6-chloropyridine-3,5-dicarbonitrile or 3-amino-5-chloropyrazine-2,6-dicarbonitrile (22.4 mmol) and $CuCl_2$ (33.6 mmol) in dry CH_3CN (200 mL), isoamilnitrite was added (33.6 mmol). The mixture was heated at 65 °C for 5 h (10 h for **1b**). The solution was acidified (HCl, 2 N) to pH=3 and extracted with CH_2Cl_2 (3×50 mL) and dried with Na_2SO_4. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography using CH_2Cl_2 as eluent to yield **1a**,**b**.

3.1.1. 2,6-Dichloropyridine-3,5-dicarbonitrile (1a). (96%). Mp 198–200 °C. Lit[22] 210–214 °C. IR (KBr, cm^{-1}): 2740 (CN). ^1H NMR ($CDCl_3$): 8.27 (s, CH). ^{13}CNMR ($CDCl_3$): 110.3 (C3, C5); 112.2 (CN); 146.9 (C4); 155.7 (C2, C6). MS (EI, *m/z* %): 197 (M^+, 100); 162 (M^+-Cl, 59). Anal. calcd for $C_7HCl_2N_3$ C, 42.46; H, 0.51; N, 21.22. Found C, 42.63; H, 0.60; N, 21.33.

3.1.2. 3,5-Dichloro-pyrazine-2,6-dicarbonitrile (1b). (84%). Mp 177–179 °C. IR (KBr, cm^{-1}): 2361–2342 (CN). ^{13}C NMR (CD_3COCD_3): 113.33 (CN); 129.69 (CCN); 153.23 (CCl). MS (EI, *m/z* %): 198 (M^+, 100); 200 (M^++2, 62). Anal. calcd for $C_6Cl_2N_4$ C, 36.21; N, 28.15. Found C, 36.32; N, 28.01.

3.2. Synthesis of diethyl 3,5-diaminodithieno[3′,2′-*e*:2,3-*b*]pyridine-2,6-dicarboxylate (2a) and diethyl 3,5-diaminodithieno[3′,2′-*e*:2,3-*b*]]pyrazine-2,6-dicarboxylate (2b)

To a solution of **1a** or **1b** (18.27 mmol) and ethyl tioglycolate (43.7 mmol) in a mixture of EtOH/THF (5:1) (240 mL), K_2CO_3 (43.7 mmol) was added, and the mixture was refluxed for 1 h. After cooling, the solid was filtered and washed with water. The product is pure enough to be used in the next step, but it can be purified by recristallization from EtOH/DMF (**2a**) or purified by flash chromatography using CH_2Cl_2 as eluent to yield **2b**.

3.2.1. Diethyl 3,5-diaminodithieno[3′,2′-*e*:2,3-*b*]pyridine-2,6-dicarboxylate (2a). (6.0 g, 90%). Mp >300. IR (KBr, cm^{-1}): 3378, 3280 (NH_2), 1678 (C=O). ^1H NMR (DMSO): 9.09 (s, 1H, CH); 7.09 (s, 4H, NH_2); 4.26 (q, 4H, OCH_2, *J*=7.1 Hz); 1.29 (t, 6H, OCH_2CH_3, *J*=7.1 Hz). ^{13}C NMR (DMSO): 17.73 (OCH_2CH_3); 60.52 (OCH_2); 93.89; 123.13; 127.05 (CH); 148.18; 161.18; 164.55. MS (IE, *m/z* %): 365 (M^+, 100). Anal. calcd for $C_{15}H_{15}N_3O_4S_2$, C, 49.30; H, 4.14; N, 11.50; S, 17.55. Found C, 49.59; H, 4.21; N,11.26; S, 17.31.

3.2.2. Diethyl 3,5-diaminodithieno[3′,2′-*e*:2,3-*b*]pyrazine-2,6-dicarboxylate (2b). (55%). Mp 240–242 °C. IR (KBr, cm^{-1}): 3474–3330 (NH_2), 1680 (C=O). ^1H NMR (CD_3Cl): 6.24 (s, 4H, NH_2); 4.41 (q, 4H, OCH_2, *J*=7.1 Hz); 1.44 (t, 6H, CH_3, *J*=7.1 Hz). ^{13}C NMR (CD_3Cl): 14.45 (CH_3); 61.06 (OCH_2); 99.63; 138.30; 144.71; 155.85; 164.85. MS (EI, *m/z* %) 366 (M^+, 100). Anal. calcd for $C_{14}H_{14}N_4O_4S_2$: C, 45.89; H, 3.85; N, 15.29; S, 17.50. Found C, 46.13; H, 3.72; N, 14.96; S, 17.54.

3.2.3. Synthesis of diethyl 3,5-di[(trifenilfosforanilidene) amino]ditieno[3′,2′-*e*:2,3-*b*]pyridine-2,6-dicarboxylate (3a). *Method A*. A solution of the **2a** (0.2 g, 0.55 mmol) triphenylphosphine (0.43 g, 1.64 mmol), hexachloroethane (0.39 g, 1.64 mmol) and triethylamine (0.28 g, 2.74 mmol) in toluene (3 mL), was heated in a sealed tube at 100 °C for 48 h. After cooling, the solid formed was filtered off, washed with water and recrystallized from EtOH/CH_2Cl_2, to yield **3a** (0.39 g, 80%).

Method B. A mixture of **2a** (1.5 g, 4.11 mmol), triphenylphosphine (3.23 g, 12.3 mmol), hexachloroethane (2.92 g, 12.3 mmol) and triethylamine (2.07 g, 20.5 mmol) in dry THF (60 mL), was heated in a sealed tube at 60 °C for 48 h. After cooling, the solid formed was filtered off and washed with THF, and the filtrate and the washings were combined and evaporated. The solid obtained was purified by flash chromatography using CH_2Cl_2/AcOEt as eluent to yield **3a** (3.5 g, 96%). Mp 265–266 °C; IR (KBr. cm^{-1}): 1686 (C=O), 1542, 1376, 1194, 527. ^1H NMR ($CDCl_3$): 8.80 (s, 1H, CH); 7.42 (m, 30H, Ph); 3.80 (q, 4H, OCH_2, *J*=7.1 Hz); 1.00 (t, 6H, CH_3, *J*=7.1 Hz). ^{13}C NMR ($CDCl_3$): 14.35 (OCH_2CH_3); 59.47 (OCH_2); 128.11; 128.36; 128.68; 130.85; 131.22; 131.20; 131.29; 131.45; 132.35; 132.55; 133.54; 134.58; 149.67; 161.12; 163.38. ^{31}P NMR ($CDCl_3$): 8.26. MS (FAB, *m/z* %): 886 (MH^+, 9);. Anal. calcd for $C_{51}H_{41}N_3O_4P_2S_2$ C, 69.14; H, 4.66; N, 4.74; S, 7.24. Found C, 68.85; H, 4.65; N, 4.70; S, 7.35.

3.2.4. Synthesis of diethyl 3,5-di[(triphenylphosphoranylidene)amino]ditieno[3′,2′-*e*:2,3-*b*]pyrazine-2,6-dicarboxylate (3b). A mixture of the heterocyclic amine **2b** (0.2 g, 0.55 mmol) triphenylphosphine (0.43 g, 1.64 mmol), hexachloroethane (0.39 g, 1.64 mmol) and triethylamine (0.28 g, 2.74 mmol) in toluene (3 mL), was heated in a sealed tube at 100 °C for 48 h. After cooling, the solid formed was filtered off, washed with water and recrystallized from EtOH/CH_2Cl_2, to yield **3b** (0.40 g, 84%). Mp 269–271 °C. IR (KBr, cm^{-1}): 1699 (C=O), 1524, 1437, 1222, 1183, 721. ^1H NMR ($CDCl_3$): 7.24–7.97 (m, 30H, Ph); 3.83 (q, 4H, OCH_2, *J*=7.1 Hz); 1.08 (t, 6H, CH_3, *J*=7.1 Hz). ^{13}C NMR ($CDCl_3$): 14.36 (CH_3); 59.80 (OCH_2); 88.45; 110.79; 128.05; 128.29; 130.97; 131.24; 131.29; 132.82; 133.02; 145.66; 148.79; 154.43; 163.51; 163.54. ^{31}P NMR ($CDCl_3$): 5.53. MS (FAB, *m/z* %) 887 (MH^+, 30); 279 (100). Anal. calcd for $C_{50}H_{40}N_4O_4P_2S_2$ C, 67.71; H, 4.55; N, 6.32; S, 7.23. Found C, 67.53; H, 4.50; N, 6.31; S, 7.35.

3.3. Synthesis of diethyl 3,5-bis(arylimino-methylenamino)dithieno[3′,2′-*e*:2,3-*b*]pyridine(or pyrazine)-2,6-dicarboxylate (4a–e)

To a solution of **3** (0.23 mmol) in CH_2Cl_2 (10 mL) (THF for **3b**) was added the appropriate isocyanate (0.54 mmol). After the mixture was stirred at room temperature for 3–5 h (*p*-tolylisocyanate: reflux). The solvent was evaporated, ether (5 mL) was added, and the mixture was stirred at room temperature for 0.5 h. The solid formed was filtered off and purified by flash chromatography using hexanes/CH_2Cl_2 (1:1 v/v) as eluent.

3.3.1. Diethyl 3,5-bis(phenyliminomethyleneamino)dithieno[3′,2′-*e*:2,3-*b*]pyridine-2,6-dicarboxylate (4a). (54%). Mp 200–203 °C. IR (KBr, cm^{-1}): 2150 (NCN); 1706 (CO); 1460; 1259; 760. ^1H NMR ($CDCl_3$): 8.79 (s, 1H, CH); 7.27 (m, 10H, Ph); 4.40 (q, 4H, OCH_2, J=7.1 Hz); 1.39 (t, 6H, CH_3, J=7.1 Hz). ^{13}C NMR ($CDCl_3$): 14.31 (CH_3); 61.89 (OCH_2); 118.40; 124.76; 15.48; 125.96; 126.71; 127.64; 129.42; 134.34; 136.49; 160.09; 162.19. Anal. calcd for $C_{29}H_{21}N_5O_4S_2$ C, 61.36; H, 3.73; N, 12.34; S, 11.30. Found C, 61.50; H, 3.98; N, 12.51; S, 11.63.

3.3.2. Diethyl 3,5-bis(4-chlorophenyliminomethyleneamino)dithieno[3′,2′-*e*:2,3-*b*]pyridine-2,6-dicarboxylate (4b). (53%). Mp 174–175 °C. IR (KBr, cm^{-1}): 2158 (NCN); 1698 (C═O); 1258; 827. ^1H NMR ($CDCl_3$): 8.75 (s, 1H, CH); 7.32 (m, 8H, Ph); 4.40 (q, 4H, OCH_2, J=7.1 Hz); 1.39 (t, 6H, CH_3, J=7.1 Hz). RMN ^{13}C ($CDCl_3$): 14.29 (CH_3); 61.84 (OCH_2); 118.49; 126.00; 126.61; 127.46; 129.52; 129.79; 131.42; 134.04; 135.19; 160.06; 162.18. MS (FAB, *m/z* %): 636 (MH^+, 2). Anal. calcd for $C_{29}H_{19}Cl_2N_5O_4S_2$ C, 54.72; H, 3.01; N, 11.00; S, 10.08. Found C, 54.84; H, 3.05; N, 10.84; S, 10.09

3.3.3. Diethyl 3,5-bis(4-methylphenyliminomethyleneamino)dithieno[3′,2′-*e*:2,3-*b*]pyridine-2,6-dicarboxylate (4c). (63%). Mp 160–162 °C. IR (KBr, cm^{-1}): 2151 (NCN); 1697 (C═O); 1467; 1261; 558. ^1H NMR ($CDCl_3$): 8.81 (s, 1H, CH); 7.23 (m, 8H, Ph); 4.40 (q, 4H, OCH_2, J=7.1 Hz); 2.35 (s, 6H, CH_3); 1.39 (t, 6H, OCH_2CH_3, J=7.1 Hz). ^{13}C NMR ($CDCl_3$): 14.32 (CH_3); 21.04 (CH_3); 61.75 (OCH_3); 124.57; 126.78; 127.53; 127.73; 129.50; 130.01; 133.56; 134.75; 135.86; 162.22. Anal. calcd for $C_{31}H_{25}N_5O_4S_2$ C, 62.50; H, 4.23; N, 11.76; S, 10.77. Found C, 62.70; H, 4.36; N, 11.53; S, 10.31

3.3.4. Diethyl 3,5-bis(4-methoxyphenylimino-methyleneamino)dithieno[3′,2′-*e*:2,3-*b*]pyridine-2,6-dicarboxylate (4d). (56%). Mp 155 °C. IR (KBr, cm^{-1}): 2150 (NCN); 1698 (C═O); 1500; 1247; 830. ^1H NMR ($CDCl_3$): 8.78 (s, 1H, CH); 6.93 (m, 8H, Ph); 4.4 (q, 4H, OCH_2, J=7.1 Hz); 3.82 (s, 6H, CH_3); 1.39 (t, 6H, OCH_2CH_3, J=7.1 Hz). ^{13}C NMR ($CDCl_3$): 14.33 (CH_3); 55.48 (CH_3); 61.69 (OCH_2); 114.67; 117.84; 125.88; 126.75; 127.00; 127.68; 128.78; 129.47; 135.13; 157.75; 160.13; 162.25. Anal. calcd for $C_{31}H_{25}N_5O_6S_2$ C, 59.32; H, 4.01; N, 11.16; S, 10.22. Found C, 58.98; H, 3.93; N, 10.99; S, 10.14.

3.3.5. Diethyl 3,5-bis(phenyliminomethyleneamino)dithieno[3′,2′-*e*:2,3-*b*]pyrazine-2,6-dicarboxylate (4e). (75%). Mp 165–167 °C. IR (KBr, cm^{-1}): 2152 (NCN); 1686 (CO); 1228, 1061, 752. ^1H NMR ($CDCl_3$): 7.11–7.45 (m, 10H, Ph); 4.50 (q, 4H, OCH_2, J=7.1 Hz); 1.45 (t, 6H, CH_3, J=7.1 Hz). ^{13}C NMR ($CDCl_3$): 14.26 (CH_3); 62.18 (OCH_2); 124.92, 125.92, 129.34 (Ph); 122.23; 134.79; 136.11; 142.50; 153.84; 161.53. Anal. calcd for $C_{28}H_{20}N_6O_4S_2$ C, 59.14; H, 3.55; N, 14.78; S, 11.28. Found C, 58.87; H, 3.34; N,14.46; S, 11.52.

3.4. Synthesis of diethyl dithieno[3′,2′-*e*:2,3-*b*]pyridine-2,6-dicarboxylates (5a–f)

A solution of the appropriate isocyanate (0.55 mmol) and **3a** (0.2 g, 0.23 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred at room temperature (*p*-tolylisocyanate: reflux) until the iminophosphorane had disappeared (TLC monitored) and it was therefore treated with an appropriate amine (0.55 mmol). The resultant solution was stirred at room temperature for 2 h. The solvent was evaporated, ether (5 mL) was added, and the mixture was stirred at room temperature for 0.5 h. The solid formed was filtered off and purified by recristallization from $EtOH/CH_2Cl_2$.

3.4.1. Diethyl 3,5-bis[anilino(thiomorpholino)methyleneamino]dithieno[3′,2′-*e*:2,3-*b*]pyridine-2,6-dicarboxylate (5a). (60%). Mp >300 °C. IR (KBr, cm^{-1}): 3329 (NH), 1687 (C═O), 1624, 1230, 1052, 933. ^1H NMR ($CDCl_3$): 8.28 (s, 1H, CH); 7.11 (m, 10H, Ph); 6.92 (br s, 2H, NH); 4.25 (m, 4H, OCH_2); 3.84 (m, 8H, H_2CNCH_2); 2.76 (m, 8H, H_2CSCH_2); 1.27 (m, 6H, CH_3). ^{13}C NMR ($CDCl_3$): 30.21 (SCH_2); 49.50 (NCH_2); 66.00 (OCH_2); 115.77; 125.38; 126.38; 128.65; 128.79; 129.05; 136.73; 149.75; 157.47; 158.89; 163.93. MS (FAB, *m/z* %): 774 (MH^+, 22). Anal. calcd for $C_{37}H_{39}N_7O_4S_4$ C, 57.41; H, 5.08; N, 12.67; S, 16.57. Found C, 57.64; H, 5.22; N, 12.35; S, 16.29.

3.4.2. Diethyl 3,5-bis[anilino(diethylamino)methyleneamino]dithieno[3′,2′-*e*:2,3-*b*]pyridine-2,6-dicarboxylate (5b). (55%). Mp 205–206 °C. IR (KBr, cm^{-1}): 3373–3291 (NH), 1706 (C═O), 1594, 1583, 1239, 1049. ^1H NMR ($CDCl_3$): 8.39 (s, 1H, CH); 6.73 (m, 10H, Ph); 5.77 (s, 2H, NH); 4.30 (q, 4H, OCH_2, J=7.1 Hz); 3.55 (q, 4H, NCH_2, J=7.1 Hz); 1.35 (m, 18H, CH_3). ^{13}C NMR ($CDCl_3$): 13.25 (NCH_2CH_3); 14.49 (OCH_2CH_3); 42.94 (NCH_2); 60.54 (OCH_2); 118.57; 122.18; 126.92; 128.08; 140.74; 151.89; 161.11; 163.32. MS (FAB, *m/z* %): 714 (MH^+, 53); 641 (MH^+-CO_2Et, 11). Anal. calcd for $C_{37}H_{43}N_7O_4S_2$ C, 62.25; H, 6.07; N, 13.73; S, 8.98. Found C, 62.41; H, 5.94, N, 13.50; S, 8.92.

3.4.3. Diethyl 3,5-bis[anilino(morpholino)methyleneamino]dithieno[3′,2′-*e*:2,3-*b*]pyridine-2,6-dicarboxylate (5c). (50%). Mp 210–211 °C. IR (KBr, cm^{-1}): 3320 (NH), 1702 (C═O), 1614, 1600, 1237, 1108, 1049, 966. ^1H NMR ($CDCl_3$): 8.30 (s, 1H, CH); 7.13 (m, 10H, Ph); 6.92 (s, 2H, NH); 4.23 (m, 4H, OCH_2); 3.60 (m, 8H, H_2COCH_2); 3.44 (m, 8H, H_2CNCH_2); 1.23 (m, 6H, CH_3). ^{13}C NMR ($CDCl_3$): 14.28 (CH_3); 47.62 (NCH_2); 60.84 (H_2COCH_2); 66.35 (OCH_2); 119.99; 122.90; 126.90; 127.89; 129.02; 134.91; 140.54; 153.18; 160.98; 162.86. MS (FAB, *m/z* %): 742 (MH^+, 54). Anal. calcd for $C_{37}H_{39}N_7O_6S_2$ C, 59.90; H, 5.30; N, 13.22; S, 8.64. Found C, 59.52; H, 5.38; N, 12.95; S, 8.75.

3.4.4. Diethyl 3,5-bis[4-methoxyanilino(morpholino) methyleneamino]dithieno[3′,2′-*e*:2,3-*b*]]pyridine-2,6-dicarboxylate (5d). (55%). Mp 238–239 °C. IR (KBr, cm^{-1}): 3333 (NH), 1712 (C═O), 1625, 1511, 1111, 823. ^1H NMR ($CDCl_3$): 8.25 (s, 1H, CH); 7.11 (m, 8H, Ph); 6.59 (s, 2H, NH); 4.17 (m, 4H, OCH_2,); 3.72 (m, 14H, CH_2OCH_2+ OCH_3); 3.48 (m, 8H, CH_2NCH_2); 1.24 (m, 6H, CH_3). ^{13}C NMR ($CDCl_3$): 14.31 (CH_3); 47.62 (NCH_2); 55.38 (OCH_3) 60.75 (OCH_2); 66.39 (CH_2OCH_2); 111.31; 114.24; 122.39; 127.00; 127.92; 131.97; 132.17, 133.66; 148.50; 153.95; 155.76; 151.04; 162.84. MS (FAB, *m/z* %): 802 (MH^+, 16). Anal. calcd for $C_{39}H_{43}N_7O_8S_2$ C, 58.41; H, 5.40; N, 12.23; S, 8.00. Found C, 58.15; H, 5.32; N, 11.93; S, 7.70.

3.4.5. Diethyl 3,5-bis[4-chloroanilino(piperidino)methyleneamino]dithieno[3′,2′-*e*:2,3-*b*]pyridine-2,6-dicarboxylate (5e). (54%). Mp 237–238 °C. IR (KBr, cm^{-1}): 3337 (NH), 1714 (C=O), 1620, 1233, 1053, 824. ^1H NMR ($CDCl_3$): 8.21 (s, 1H, CH); 7.13 (m, 8H, Ph); 6.60 (s, 2H, NH); 4.20 (m, 4H, OCH_2,); 3.45 (m, 8H, H_2CNCH_2); 1.39 (m, 18H, $NCH_2CH_2CH_2$+CH_3). ^{13}C NMR ($CDCl_3$): 14.30 (CH_3); 24.7 ($NCH_2CH_2CH_2$); 25.4 (NCH_2CH_2) 48.3 (NCH_2); 60.80 (OCH_2); 120.93; 127.26, 128.06; 139.70; 152.70; 161.00. MS (FAB, *m/z* %): 806 (MH^+, 16). Anal. calcd for $C_{39}H_{41}Cl_2N_7O_4S_2$ C, 58.06; H, 5.12; N, 12.15; S, 7.95. Found C, 57.94; H, 5.15; N, 11.76; S, 7.79.

3.4.6. Diethyl 3,5-bis[anilino(isopropylamino)methyleneamino]dithieno[3′,2′-*e*:2,3-*b*]pyridine-2,6-dicarboxylate (5f). (40%). Mp >300 °C. IR (KBr, cm^{-1}): 3345 (NH), 1677 (C=O), 1633, 1530, 1491, 1051. ^1H NMR ($CDCl_3$): 8.45 (s, 1H, CH); 7.35 (m, 10H, Ph); 7.08 (m, 4H, NH+NHPh); 4.29 (m, 6H, HNCH+OCH_2); 1.23 (m, 18H, $HNCH_2CH3$+OCH_2CH_3). ^{13}C NMR ($CDCl_3$): 14.34 (CH_3); 23.04 ($HNCHCH_3$); 43.33 (HNCH); 60.74 (OCH_2); 124.02, 124.57; 128.35; 128.67; 129.43; 138.68; 148.37; 149.23; 160.85; 163.17. MS (FAB, *m/z* %): 686 (MH^+, 100); 687 (MH^++1, 39); 688 (MH^++2.18). Anal. calcd for $C_{35}H_{39}N_7O_4S_2$ C, 61.29; H, 5.73; N, 14.30; S, 9.35. Found C, 61.42; H, 5.85; N, 14.41; S, 9.49.

3.5. Synthesis of pyrido(or pyrazino)[5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-diones (6a–y)

A solution of the appropriate isocyanate (0.55 mmol) and **3a** or **3b** (0.23 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred at room temperature (*p*-tolylisocyanate: reflux) until the iminophosphorane had disappeared (3 h, TLC monitored) and it was therefore treated with an appropriate amine (0.55 mmol). The resultant solution was stirred at room temperature for 2 h. The solvent was evaporated and the residue was solved in acetone (8 mL), a catalytic amount of K_2CO_3 was added, the mixture was refluxed for 0.5 h and the solid obtained was filtered off, washed with water, acetone and recrystallized from EtOH/CH_2Cl_2. Compounds **6a** and **6f** could not be purified because their insolubility in ordinary solvents.

3.5.1. 2,10-Bis(diethylamino)-3,9-diphenylpyrido[5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione (6a). (69%). Mp >300 °C. IR (KBr, cm^{-1}): 1675 (C=O), 1530, 1378, 1282, 699. MS (FAB, *m/z* %): 622 (MH^+, 10); 623 (MH^++1, 4); 550 (MH^+−diethylamine, 3).

3.5.2. 3,9-Diphenyl-2,10-dithiomorpholinpyrido[5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione (6b). (89%). Mp >300 °C. IR (KBr, cm^{-1}): 1677 (C=O), 1534, 1409. ^1H NMR ($CDCl_3$): 8.91 (s, 1H, CH); 7.47 (m, 10H, Ph); 3.62 (m, 8H, NCH_2); 2.39 (m, 8H, SCH_2). ^{13}C NMR ($CDCl_3$): 26.49 (SCH_2); 51.93 (NCH_2); 125.42; 128.64; 129.01; 135.12; 137.05; 149.68; 158.17; 159.05. MS (FAB, *m/z* %): 682 (MH^+, 4); 580 (MH^+−thiomorpholine, 4). Anal. calcd for $C_{33}H_{27}N_7O_2S_4$ C, 58.13; H, 3.99; N, 14.38; S, 18.81. Found C, 58.40; H, 4.03; N, 14.58; S, 19.02.

3.5.3. 2,10-Dimorpholino-3,9-diphenylpyrido[5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione (6c). (75%). Mp >300 °C. IR (KBr, cm^{-1}): 2856, 1677 (C=O), 1529, 1118, 918. ^1H NMR ($CDCl_3$): 8.86 (s, 1H, CH); 7.47 (m, 10H, Ph); 3.54 (m, 8H, OCH_2); 3.32 (m, 8H, NCH_2). MS (FAB, *m/z* %): 650 (MH^+, 10). Anal. calcd for $C_{33}H_{27}N_7O_4S_2$ C, 61.00; H, 4.19; N, 15.09; S, 9.87. Found C, 61.45; H, 4.18; N, 15.08; S, 9.73.

3.5.4. 3,9-Diphenyl-2,10-dipiperidinopyrido[5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione (6d). (60%). Mp >300 °C. IR (KBr, cm^{-1}): 2929, 1675 (C=O), 1589, 1532, 1251, 707. ^1H NMR ($CDCl_3$): 8.90 (s, 1H, CH); 7.42 (m, 10H, Ph); 3.30 (m, 8H, NCH_2); 1.49–1.35 (m, 12H, $NCH_2CH_2CH_2$). ^{13}C NMR ($CDCl_3$): 24.13 ($NCH_2CH_2CH_2$); 24.94 (NCH_2CH_2); 50.48 (NCH_2); 115.06; 125.49; 126.48; 128.16; 128.79; 128.98; 137.48; 150.12; 158.48; 159.22; 163.96. MS (FAB, *m/z* %): 646 (MH^+, 8). Anal. calcd $C_{35}H_{31}N_7O_2S_2$ C, 65.09; H, 4.84; N, 15.18; S, 9.93. Found C, 64.71; H, 4.83; N, 14.94; S, 10.01.

3.5.5. 3,9-Bis(4-chlorophenyl)-2,10-dimorpholinopyrido-[5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimi-dine-4,8(3*H*,9*H*)-dione (6e). (54%). Mp >300 °C. IR (KBr, cm^{-1}): 2847, 1678 (C=O), 1635, 1530, 1250, 833. ^1H NMR ($CDCl_3$): 7.46 (m, 8H, Ph); 6.40 (s, 1H, CH); 3.70 (m, 8H, OCH_2,); 3.40 (m, 8H, NCH_2); ^{13}C NMR ($CDCl_3$): 44.2 (NCH_2); 66.4 (OCH_2); 121.25; 128.30; 128.44; 128.85; 131.90; 132.09; 137.33; 154.85. Anal. calcd for $C_{33}H_{25}Cl_2N_7O_4S_2$ C, 55.15; H, 3.51; N, 13.64; S, 8.92. Found C, 55.48; H, 3.85; N, 13.54; S, 8.66.

3.5.6. 3,9-Bis(4-chlorophenyl)-2,10-dipiperidinopyrido-[5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione (6f). (67%). Mp >300 °C. IR (KBr, cm^{-1}): 2935, 1677 (C=O), 1530, 1403, 1253, 769. MS (FAB, *m/z* %) 714 (MH^+, 3); 716 (MH^++2, 3).

3.5.7. 2,10-Dimorpholino-3,9-di-*p*-tolylpyrido[5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione (6g). (77%). Mp >300 °C. IR (KBr, cm^{-1}): 2852, 2360, 1674 (C=O), 1534, 1117. ^1H NMR ($CDCl_3$): 8.84 (s, 1H, CH); 7.31 (m, 8H, Ph); 3.56 (m, 8H, OCH_2); 3.33 (m, 8H, NCH_2); 2.45 (s, 6H, Me). ^{13}C NMR ($CDCl_3$): 21.24 (Me); 49.47 (NCH_2); 66.05 (OCH_2); 115.65; 125.39; 126.24; 128.43; 129.66; 134.06; 138.58; 149.68; 157.55 Ms (FAB, *m/z* %): 678 (MH^+, 12). Anal. calcd for $C_{35}H_{31}N_7O_4S_2$ C, 62.02; H, 4.61; N, 14.47; S, 9.46. Found C, 62.13; H, 4.39; N, 14.41; S, 9.33.

3.5.8. 2,10-Dipiperidino-3,9-di-*p*-tolylpyrido[5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione (6h). (64%). Mp >300 °C. IR (KBr, cm^{-1}): 2932, 1675 (C=O), 1586, 1530, 1407, 1254, 751. ^1H NMR ($CDCl_3$): 8.96 (s, 1H, CH); 7.30 (m, 8H, Ph); 3.29 (m, 8H, NCH_2); 2.44 (s, 6H, Me); 1.35 (m, 12H, $NCH_2CH_2CH_2$). ^{13}C NMR ($CDCl_3$): 21.23 (CH_3); 24.15 ($NCH_2CH_2CH_2$); 24.98 (NCH_2CH_2); 50.41 (NCH_2); 115.10; 125.69; 126.45; 128.52; 129.47; 134.80; 138.04; 150.12; 158.55; 159.37; 164.08. MS (FAB, *m/z* %): 674 (MH^+, 8). Anal. calcd for $C_{37}H_{35}N_7O_2S_2$ C, 65.95; H, 5.24; N, 14.55; S, 9.52. Found C, 65.87; H, 5.30; N, 14.73; S, 9.59.

3.5.9. 3,9-Bis(4-methoxyphenyl)-2,10-dimorpholinopyrido[5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione (6i). (61%). Mp >300 °C. IR (KBr, cm^{-1}): 2963, 1676 (C═O), 1536, 1507, 1246, 917. ^1H NMR ($CDCl_3$): 8.66 (s, 1H, CH); 7.15 (m, 8H, Ph); 3.87 (s, 6H, OCH_3); 3.36 (m, 8H, OCH_2); 3.34 (s, 8H, NCH_2). ^{13}C NMR ($CDCl_3$): 49.49 (NCH_2); 55.47 (OCH_3); 66.12 (OCH_2); 114.14; 115.47; 125.19; 126.1; 129.85; 149.58; 157.68; 159.09; 159.36; 163.72. MS (FAB, *m/z* %): 710 (MH^+, 13). Anal. calcd for $C_{35}H_{31}N_7O_6S_2$ C, 59.22; H, 4.40; N, 13.81; S, 9.04. Found C, 59.25; H, 4.41; 13.55; S, 9.13.

3.5.10. 3,9-Bis(4-methoxyphenyl)-2,10-dipiperidinopyrido[5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione (6j). (62%). Mp >300 °C. IR (KBr, cm^{-1}): 2933, 1675 (C═O), 1532, 1511, 1251, 915. ^1H NMR ($CDCl_3$): 8.89 (s, 1H, CH); 7.13 (m, 8H, Ph); 3.88 (s, 6H, OCH_3); 3.31 (m, 8H, NCH_2); 1.45 (m, 12H, $NCH_2CH_2CH_2$). ^{13}C NMR ($CDCl_3$): 24.15 ($NCH_2CH_2CH_2$); 25.08 (NCH_2CH_2); 50.44 (NCH_2); 55.47 (OCH_3); 114.06; 115.06; 125.61; 126.41; 129.87; 130.01; 150.06; 158.68; 159.06; 159.50; 164.01. MS (FAB, *m/z* %): 706 (MH^+, 52). Anal. calcd for $C_{37}H_{35}N_7O_4S_2$ C, 62.96; H, 5.00; N, 13.89; S, 9.09. Found C, 62.46; H, 4.97; N, 13.68; S, 8.89.

3.5.11. 2,10-Bis(butylamino)-3,9-diphenylpyrido[5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione (6k). (40%). Mp >300 °C. IR (KBr, cm^{-1}): 3429–3368 (NH), 2931; 1678 (C═O), 1549, 1324, 772. ^1H NMR ($CDCl_3$): 8.93 (s, 1H, CH); 7.41 (m, 10H, Ph); 4.28 (t, 3H, NH); 3.60 (m, 4H, NCH_2); 1.61 (m, 4H, NCH_2CH_2); 1.38 (m, 4H, $NCH_2CH_2CH_2$); 1.00 (t, 6H, CH_3). ^{13}C NMR ($CDCl_3$): 13.76 (CH_3); 20.00 ($NCH_2CH_2CH_2$); 31.24 (NCH_2CH_2); 41.98 (NCH_2); 110.84; 125.61; 126.49; 129.00; 130.01; 130.62; 134.38; 151.78; 153.23; 158.44; 164.37. MS (FAB, *m/z* %): 622 (MH^+, 100). Anal. calcd for $C_{33}H_{31}N_7O_2S_2$ C; 63.75; H, 5.03; N, 15.77; S, 10.31. Found C, 63.36; H, 4.97; N, 15.54; S, 10.26.

3.5.12. 2,10-Bis(isopropylamino)-3,9-diphenylpyrido-[5″,6″:4,5:3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione (6l). (45%). Mp >300 °C. IR (KBr, cm^{-1}): 3436 (NH), 3061, 2974; 1676 (C═O), 1547, 1289, 1176, 770. ^1H NMR ($CDCl_3$): 8.89 (s, 1H, CH); 7.52 (m, 10H, Ph); 4.50 (m, 2H, NCH); 4.05 (d, 2H, HN, *J*=7.3 Hz); 1.26 (d, 12H, CH_3, *J*=6.4 Hz). ^{13}C NMR ($CDCl_3$): 22.84 (CH_3); 44.09 (NCH); 110.76; 125.55, 126.44, 129.02; 129.94; 130.57, 134.34; 151.81; 152.54; 158.45; 164.35. MS (FAB, *m/z* %): 594 (MH^+, 32). Anal. calcd for $C_{31}H_{27}N_7O_2S_2$ C, 62.71; H, 4.58; N, 16.51; S, 10.80. Found 62.61; H, 4.47; N, 16.84; S, 10.92.

3.5.13. 3,9-Bis(4-chlorophenyl)-2,10-bis(isopropylamino)pyrido[5″,6″:4,5;3″2″:4′,5″]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione (6m). (33%). Mp >300 °C. IR (KBr, cm^{-1}): 3323 (NH), 2973; 1627 (C═O), 1560, 1238. ^1H NMR (CD_3COCD_3): 7.80 (s, 1H, CH); 7.30 (m, 8H, Ph); 5.58 (d, 2H, NH, *J*=7.3 Hz); 3.87 (m, 2H, NCH,); 1.12 (d, 12H, CH_3, *J*=6.8 Hz). ^{13}C NMR (CD_3COCD_3): 23.30 (CH_3); 42.30 (NCH); 120.11; 126.17; 129.23; 140.66; 155.18; 194.49. Anal. calcd for $C_{31}H_{25}Cl_2N_7O_2S_2$ C, 56.19; H, 3.80; N, 14.80; S, 9.68. Found C, 56.58; H, 4.12; N, 14.79; S, 10.01.

3.5.14. 2,10-Bis(isopropylamino)-3,9-di-*p*-tolylpyrido-[5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione (6n). (70%). Mp >300 °C. IR (KBr, cm^{-1}): 3412 (NH), 2970; 1675 (C═O), 1546, 1320, 1176, 773. ^1H NMR ($CD_2Cl_2/CDCl_3$): 9.07 (s, 1H, CH); 7.30 (m, 8H, Ph); 4.50 (m, 2H, NCH); 4.12 (d, 2H, HN, *J*=7.8 Hz); 2.48 (s, 6H, CH_3) 1.24 (d, 12H, $NCHCH_3$, *J*=6.6 Hz). ^{13}C NMR ($CDCl_3$): 21.53 (CH_3); 22.92 (CH_3); 44.46 (NCH); 126.51; 126.92; 128.89; 131.72; 132.02; 133.61; 140.83; 152.30; 153.30; 158.97; 164.65. MS (FAB, *m/z* %): 622 (MH^+, 88). Anal. calcd for $C_{33}H_{31}N_7O_2S_2$ C, 63.75; H, 5.03; N, 15.77; S, 10.31. Found C, 63.90; H, 4.99; N, 15.64; S, 10.21.

3.5.15. 2,10-Bis(isopropylamino)-3,9-bis(4-methoxyphenyl)pyrido[5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione (6o). (86%). Mp >300 °C. IR (KBr, cm^{-1}): 3383–3428 (NH), 2967; 1674 (C═O), 1511, 1246, 1039, 771. ^1H NMR (CD_5N): 9.71 (s, 1H, CH); 7.44 (m, 4H, Ph); 6.90 (m, 4H, Ph); 6.29 (d, 2H, HN, *J*=8.3 Hz); 4.70 (m, 2H, NCH,); 3.52 (s, 6H, OCH_3); 1.20 (d, 12H, $NCHCH_3$, *J*=6.8 Hz). MS (FAB, *m/z* %): 654 (MH^+, 10). Anal. calcd for $C_{33}H_{31}N_7O_4S_2$ C, 60.63; H, 4.78; N, 15.00; S, 9.81. Found C, 60.55; H, 4.70; N, 14.59; S, 9.62.

3.5.16. 3,9-Diphenyl-2,10-dithiomorpholinopyrazino-[5″,6″:4,5:3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione (6p). (30%). Mp >300 °C. IR (KBr, cm^{-1}): 2911, 1678 (C═O), 1531, 1197, 761. ^1H NMR ($CDCl_3$): 7.41–7.63 (m, 10H, Ph); 3.67 (m, 8H, NCH_2); 2.35 (m, 8H, SCH_2). ^{13}C NMR ($CDCl_3$): 26.39 (SCH_2); 51.86 (NCH_2); 128.67, 128.93, 129.41 (Ph); 137.04; 158.48; 159.36. MS (FAB, *m/z* %): 683 (MH^+, 10). Anal. calcd for $C_{32}H_{26}N_8O_2S_4$: C, 56.28; H, 3.84; N, 16.41; S, 18.78. Found C, 56.34; H, 4.03; N, 16.58; S, 19.02.

3.5.17. 2,10-Dimorpholino-3,9-diphenylpyrazino[5″,6″:4,5:3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione (6q). (40%). Mp >300 °C. IR (KBr, cm^{-1}): 2855, 2368, 1679 (C═O), 1532, 1200, 922. ^1H NMR ($CDCl_3$): 7.45–7.61 (m, 10H, Ph); 3.51 (m, 8H, OCH_2); 3.36 (m, 8H, NCH_2). ^{13}C NMR ($CDCl_3$): 49.36 (NCH_2); 65.93 (OCH_2); 128.34, 128.96, 129.37 (Ph); 136.75; 142.21; 148.47; 157.72; 159.23. MS (FAB, *m/z* %): 651 (MH^+, 85); (MH^+−morpholine, 40). Anal. calcd for $C_{32}H_{26}N_8O_4S_2$: C, 59.06; H, 4.03; N, 17.22; S, 9.86. Found C, 58.72; H, 3.94; N, 17.62; S, 9.80.

3.5.18. 3,9-Diphenyl-2,10-dipiperidinopyrazino[5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione (6r). (30%). Mp >300 °C. IR (KBr, cm^{-1}): 2934, 1678 (C═O), 1531, 1193, 922. ^1H NMR ($CDCl_3$): 7.41–7.59 (m, 10H, Ph); 3.34–1.31 (m, 12H, $NCH_2CH_2CH_2$). ^{13}C NMR ($CDCl_3$): 23.96 ($NCH_2CH_2CH_2$); 24.84 (NCH_2CH_2); 50.35 (NCH_2); 128.52, 128.47, 129.12 (Ph); 118.74; 137.45; 142.24; 148.82; 157.78; 158.78; 159.57. MS (FAB, *m/z* %): 647 (MH^+, 100); 648 (MH^++1, 50). Anal. calcd for $C_{34}H_{30}N_8O_2S_2$: C, 63.14; H, 4.68; N, 17.32; S, 9.92. Found C, 63.12; H, 4.59; N, 17.28; S, 9.77.

3.5.19. 2,10-Bis(isopropylamino)-3,9-diphenylpyrazino-[5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione (6s). (46%). Mp >300 °C. IR (KBr,

cm^{-1}): 3431 (NH), 1678 (C=O), 1548, 1200, 759. ^{1}H NMR ($CDCl_3$): 7.26–7.72 (m, 10H, Ph); 4.64 (m, 2H, NCH); 4.13 (d, 2H, HN, J=8.3 Hz); 1.21 (d, 12H, CH_3, J=6.8 Hz). ^{13}C NMR ($CDCl_3$): 22.89 ($NCHCH_3$); 44.10 (NCH); 128.63, 130.36, 130.88 (Ph); 120.68; 129.15; 134.05; 142.11; 150.32; 152.19; 158.67 MS (FAB, *m/z* %): 595 (MH^+, 100); 596 (MH^++1, 50). Anal. calcd for $C_{30}H_{26}N_8O_2S_2$ C, 60.59; H, 4.41; N, 18.84; S, 10.78. Found C, 60.69; H, 4.14; N, 18.62; S, 10.53.

3.5.20. 3,9-Bis(4-chlorophenyl)-2,10-dimorpholinopyrazino[5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]di-pyrimidine-4,8(3*H*,9*H*)-dione (6t). (27%). Mp >300 °C. IR (KBr, cm^{-1}): 2962, 2855, 1680 (C=O), 1533, 1201, 922. ^{1}H NMR ($CDCl_3$): 7.39–7.57 (m, 8H, Ph); 3.56 (m, 8H, OCH_2,); 3.36 (m, 8H, NCH_2); ^{13}C NMR ($CDCl_3$): 49.43 (NCH_2); 65.96 (OCH_2); 129.59, 129.70 (Ph); 134.96; 135.02; 142.04; 148.38; 157.52; 157.56; 158.98. MS (FAB, *m/z* %): 719 (MH^+, 5); 217 (100). Anal. calcd for $C_{32}H_{24}Cl_2N_8O_4S_2$: C, 53.41; H, 3.36; N, 15.57; S, 8.91. Found C, 53.48; H, 3.35; N, 15.74; S, 8.61.

3.5.21. 3,9-Bis(4-chlorophenyl)-2,10-dipiperidinopyrazino[5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]di-pyrimidine-4,8(3*H*,9*H*)-dione (6u). (42%). Mp >300 °C. IR (KBr, cm^{-1}): 2937, 1675 (C=O), 1530, 1193, 1092. ^{1}H NMR ($CDCl_3$): 7.26–7.55 (m, 8H, Ph); 3.32 (m, 8H, NCH_2); 1.26–1.50 (m, 12H, $NCH_2CH_2CH_2$). ^{13}C NMR ($CDCl_3$): 23.89 ($NCH_2CH_2CH_2$); 24.88 (NCH_2CH_2); 50.39 (NCH_2); 129.33, 129.85 (Ph); 118.79; 134.42; 135.75; 142.12; 148.74; 157.78; 158.56; 159.30. MS (FAB, *m/z* %) 715 (MH^+, 5). Anal. calcd for $C_{34}H_{28}Cl_2N_8O_2S_2$ C, 57.06; H, 3.94; N, 15.66; S, 8.96. Found C, 57.30; H, 3.96; N, 15.29; S, 9.10.

3.5.22. 2,10-Dimorpholino-3,9-di-*p*-tolylpyrazino [5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione (6v). (27%). Mp >300 °C. IR (KBr, cm^{-1}): 2963, 2853, 1679 (C=O), 1530. ^{1}H NMR ($CDCl_3$): 7.27–7.35 (m, 8H, Ph); 3.52 (m, 8H, OCH_2); 3.37 (m, 8H, NCH_2); 2.46 (s, 6H, Me). ^{13}C NMR ($CDCl_3$): 21.28 (Me); 49.32 (NCH_2); 65.97 (OCH_2); 127.97, 129.96 (Ph); 119.60; 120.19; 134.07; 139.05; 142.32; 148.48; 157.76; 159.38. MS (FAB, *m/z* %): 679 (MH^+, 60); 592 (MH^+−morpholine, 30). Anal. calcd for $C_{34}H_{30}N_8O_4S_2$ C, 60.16; H, 4.45; N, 16.51; S, 9.45. Found C, 60.13; H, 4.39; N, 16.41; S, 9.33.

3.5.23. 2,10-Dipiperidino-3,9-di-*p*-tolylpyrazino [5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione (6w). (28%). Mp >300 °C. IR (KBr, cm^{-1}): 2935, 1678 (C=O), 1529, 1119. ^{1}H NMR ($CDCl_3$): 7.27–7.32 (m, 8H, Ph); 3.31–3.36 (m, 8H, NCH_2); 2.45 (s, 6H, Me); 1.49–1.34 (m, 12H, $NCH_2CH_2CH_2$). ^{13}C NMR ($CDCl_3$): 21.24 (Me); 24.00 ($NCH_2CH_2CH_2$); 24.88 (NCH_2CH_2); 50.31 (NCH_2); 128.16, 129.74 (Ph); 118.70; 134.77; 138.45; 142.28; 148.78; 158.89; 159.72. MS (FAB, *m/z* %): 675 (MH^+, 95); 590 (M^+−piperidine, 40). Anal. calcd for $C_{36}H_{34}N_8O_2S_2$: C, 64.07; H, 5.08; N, 16.60; S, 9.50. Found C, 64.17; H, 5.20; N, 16.73; S, 9.59.

3.5.24. 3,9-Bis(4-methoxyphenyl)-2,10-dimorpholino-pyrazino[5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione (6x). (28%). Mp >300 °C. IR (KBr, cm^{-1}): 2960, 1680 (C=O), 1508, 1521, 1249. ^{1}H NMR ($CDCl_3$): 7.04–7.39 (m, 8H, Ph); 3.89 (s, 6H, OMe); 3.54 (m, 8H, OCH_2); 3.37 (s, 8H, NCH_2). ^{13}C NMR ($CDCl_3$): 49.36 (NCH_2); 55.57 (OCH_3); 66.05 (OCH_2); 114.56, 129.34 (Ph); 119.55; 129.34; 142.21; 148.37; 157.75; 157.93; 159.50; 159.59. MS (FAB, *m/z* %): 711 (MH^+, 85); (MH^+−morpholine, 15). Anal. calcd for $C_{34}H_{30}N_8O_6S_2$ C, 57.45; H, 4.25; N, 15.76; S, 9.02. Found C, 57.82; H, 3.96; N, 15.59; S, 8.96.

3.5.25. 3,9-Bis(4-methoxyphenyl)-2,10-dipiperidino-pyrazino[5″,6″:4,5;3″2″:4′,5′]dithieno[3,2-*d*:3′,2′-*d*′]dipyrimidine-4,8(3*H*,9*H*)-dione (6y). (26%). Mp >300 °C. IR (KBr, cm^{-1}): 2934, 1679 (C=O), 1508, 1530, 1252, 1190, 920. ^{1}H NMR ($CDCl_3$): 7.02–7.39 (m, 8H, Ph); 3.89 (s, 6H, OCH_3); 3.34–3.37 (m, 8H, NCH_2); 1.35–1.48 (m, 12H, $NCH_2CH_2CH_2$). ^{13}C NMR ($CDCl_3$): 24.02 ($NCH_2CH_2CH_2$); 24.99 (NCH_2CH_2); 50.32 (NCH_2); 55.54 (OCH_3); 114.64, 129.48 (Ph); 118.68; 129.97; 142.35; 148.78; 157.75; 158.93; 159.26; 159.86. MS (FAB, *m/z* %): 707 (MH^+, 90). Anal. calcd for $C_{36}H_{34}N_8O_4S_2$ C, 61.17; H, 4.85; N, 15.85; S, 9.07. Found C, 61.46; H, 4.97; N, 15.68; S, 8.89.

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