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Synthesis and Antibacterial Activity of Some New Ethyl Thionicotinates, Thieno[2,3-*b*]pyridines, Pyrido[3',2':4,5] thieno[3,2-*d*]pyrimidines, and Pyrido[3',2':4,5]thieno[3,2-*d*][1,2,3]triazines Containing Sulfonamide Moieties

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SYNTHESIS AND ANTIBACTERIAL ACTIVITY OF SOME NEW ETHYL THIONICOTINATES, THIENO[2,3-*b*]PYRIDINES, PYRIDO[3',2':4,5]THIENO[3,2-*d*]PYRIMIDINES, AND PYRIDO[3',2':4,5]THIENO[3,2-*d*][1,2,3]TRIAZINES CONTAINING SULFONAMIDE MOIETIES

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*Ethyl 5-cyano-6-mercaptopnicotinate derivatives 1a,b reacted with the N-[4-(aminosulfonyl)phenyl]-2-chloroacetamide derivatives 2a,b to give the ethyl 6-[(2-{[4-(aminosulfonyl)phenyl]amino}-2-oxoethyl)thio]nicotinate derivatives 3a–d. Cyclization of 3a–d afforded the corresponding ethyl 3-amino-2-([4-(aminosulfonyl)phenyl]amino)carbonylthieno[2,3-*b*]pyridine-5-carboxylate derivatives 4a–d. Ethyl 3-[4-(amino-sulfonyl)phenyl]-4-oxopyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine-8-carboxylate derivatives 5a–d and ethyl 3-[4-(amino-sulfonyl)phenyl]-4-oxopyrido[3',2':4,5]thieno[3,2-*d*][1,2,3]-triazine-8-carboxylate derivatives 6a–d were prepared from 4a–d. Reaction of 1a,b with chloroacetonitrile (7) and condensation of the thus formed 3-aminothienopyridines 8a,b with dimethylformamide-dimethylacetal (DMF-DMA) yielded the corresponding ethyl 2-cyano-3-[(N,N-dimethylamino)methylene]amino]thieno[2,3-*b*]pyridine-5-carboxylate derivatives 9a,b. Reaction of compounds 9a,b with the sulfadiazine (10) gave ethyl 4-{[4-(amino-sulfonyl)phenyl]amino}pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine-8-carboxylate derivatives 12a,b. Antibacterial activity was screened for some of the newly synthesized compounds.*

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Keywords Antibacterial; ethyl thionicotinates; pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidines; pyrido[3',2':4,5]thieno[3,2-*d*][1,2,3]triazines; sulfonamides; thieno[2,3-*b*]pyridines

INTRODUCTION

Aromatic sulfonamide derivatives exhibit a wide range of bioactivities, including antiangiogenic,¹ antitumor,^{2,3} anti-inflammatory,^{4,5} antianalgesic,^{4,5} antidiabetic,⁶ antitubercular,⁷ antiglaucoma,⁸ anti-HIV-1⁹, anti-HIV-2,¹⁰ cytotoxic,¹¹ antihypertensive,¹²

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antimicrobial,¹³ and antimalarial¹⁴ agents and cyclin-dependent kinase inhibitors.¹⁵ Furthermore, *S*-substituted thiopyridines possess neurotropic,¹⁶ cardiovascular,¹⁷ and antimicrobial¹⁸ activities and are used as adenosine receptor ligands.¹⁹ Also, ethyl nicotinate derivatives have been reported to be used as agrochemical fungicides²⁰ and anticancer²¹ agents. Moreover, thieno[2,3-*b*]pyridines possess a wide range of biological activities such as antiviral,^{22,23} antidiabetic,²⁴ antimicrobial,^{18,25,26} anti-inflammatory,²⁷ antitumor,²⁸ antiparasitic,²⁹ and neurotropic¹⁶ activities. Furthermore, pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidines have been reported to have antiallergic,³⁰ antiprotozoal,³¹ antianaphylactic,³² and antimicrobial^{18,25,26} activities. On the other hand, pyridothienotriazines have been used as antiprotozoal,^{31,33} antitumor,³⁴ antiangiogenic,³⁵ and antimicrobial¹⁸ agents and have been reported to inhibit NO and eicosanoid biosynthesis.³⁶ The above findings, and in continuation of our research in the chemistry of sulfonamides^{37–39} and fused pyridines,^{40–46} have stimulated interest for the synthesis of new derivatives that are required in medicinal chemistry programs.

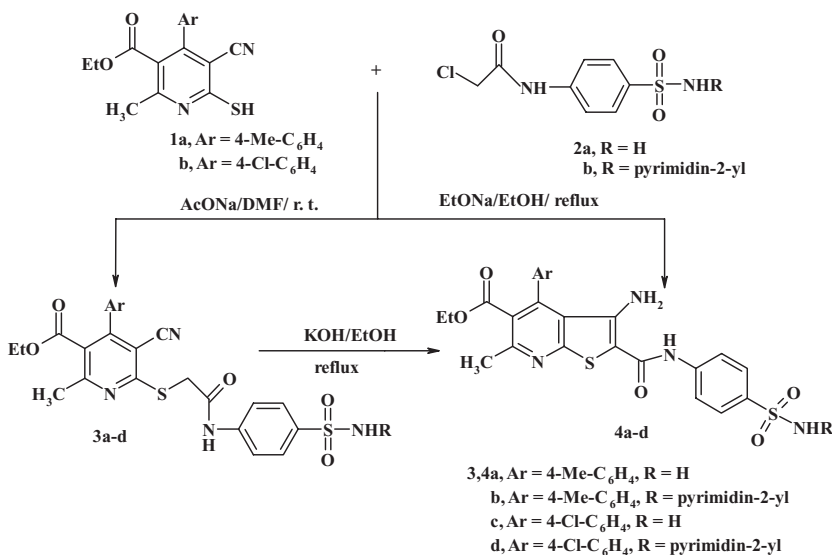
RESULTS AND DISCUSSION

Ethyl 5-cyano-6-mercapto-2-methyl-4-(4-methylphenyl)nicotinate (**1a**)⁴⁷ reacted with *N*-[4-(aminosulfonyl)phenyl]-2-chloroacetamide (**2a**)⁴⁸ in DMF/AcONa solution under stirring at room temperature to give the ethyl 5-cyano-6-[(2-{[4-(aminosulfonyl)phenyl]amino}-2-oxoethyl)thio]nicotinate derivative **3a** in good yield. The IR spectrum of **3a** indicated the presence of CN, NH₂, and two CO groups, and its ¹H NMR spectrum revealed SCH₂ protons at $\delta = 4.21$ ppm. Similarly **1a** reacted with 2-chloro-*N*-[4-[(pyrimidin-2-yl amino)sulfonyl]phenyl]acetamide (**2b**)⁴⁸ to yield the corresponding ethyl 5-cyano-6-{[2-oxo-2-(4-[(pyrimidin-2-ylamino)sulfonyl]phenyl)amino]ethyl}thio}nicotinate derivative **3b** in good yield. The IR and ¹H NMR spectra of **3b** were found to be in good agreement with the assigned structure. In the same way, **1b**⁴⁹ reacted with **2a,b** to afford the corresponding ethyl 5-cyano-6-[(2-{[4-(aminosulfonyl)phenyl]amino}-2-oxoethyl)thio]nicotinate derivatives **3c,d** in good yield. The IR spectra of **3c,d** indicated the presence of CN, NH₂, and two CO groups, while its ¹H NMR spectra revealed the signals of SCH₂ at $\delta = 4.28$ and 4.23 ppm, in addition to the other signals.

The structures of **3a–d** were further elucidated via elemental analysis and their cyclization into the corresponding ethyl 3-amino-2-([4-(aminosulfonyl)phenyl]amino)-carbonylthieno[2,3-*b*]pyridine-5-carboxylate derivatives **4a–d** upon treatment with ethanolic potassium hydroxide under reflux. The structures of **4a–d** were confirmed based on elemental analysis and spectral data. The IR spectra of **4a–d** indicated the absence of CN group instead of the newly born NH₂ group was detected, while its ¹H NMR spectra revealed the protons of the newly NH₂ and absence of any signals that might be attributed to SCH₂ protons (see Scheme 1 and the Experimental section).

Unequivocal support for the structure of **4a–d** was achieved via its synthesis through an alternate route via the reaction between **1a,b** and **2a,b** in ethanolic sodium ethoxide solution under reflux (see Scheme 1 and the Experimental section).

Compound **4a** reacted with acetic anhydride in glacial acetic acid under reflux to afford a reaction product that corresponded to equimolecular addition of the reagent to **4a** followed by loss of one molecule of acetic acid. The IR spectrum of the reaction product showed the absorption bands of two carbonyl groups at 1731 and 1628 cm⁻¹ and NH₂ at 3487, 3326 cm⁻¹, while its ¹H NMR spectrum revealed the disappearance of NH₂ and NH



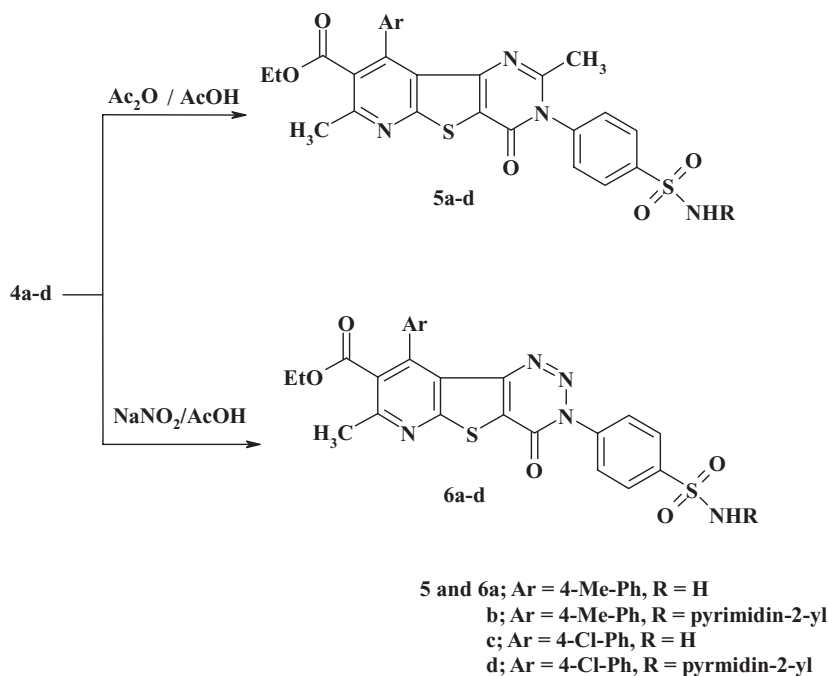
Scheme 1

protons, and instead of the protons of CH₃ group, on position 2 of the pyrimidine ring was detected at $\delta = 2.65$ ppm. Based on the above data and the elemental analysis, the reaction product could be formulated as the ethyl 3-[4-(aminosulfonyl)phenyl]-2,7-dimethyl-9-(4-methylphenyl)-4-oxo-3,4-dihydropyrido[3',2':4,5]thieno[3,2-*b*]pyrimidine-8-carboxylate (**5a**). Similarly, **4b-d** reacted with acetic anhydride in glacial acetic acid to give the corresponding ethyl 3-[4-(aminosulfonyl)phenyl]-2,7-dimethyl-4-oxo-3,4-dihydropyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine-8-carboxylate derivatives **5c-d**. The structure of **5a-d** was elucidated via elemental analysis and spectral studies (see Scheme 2 and the Experimental section).

Diazotization and self coupling of compounds **4a-d** afforded the corresponding ethyl 3-[4-(aminosulfonyl)phenyl]-7-methyl-4-oxo-3,4-dihydropyrido[3',2':4,5]thieno[3,2-*b*]-[1,2,3]triazine-8-carboxylate derivatives **6a-d**. ¹H NMR spectra of **6a-d** revealed the absence of the signals corresponding to NH and NH₂ protons (see Scheme 2 and the Experimental section).

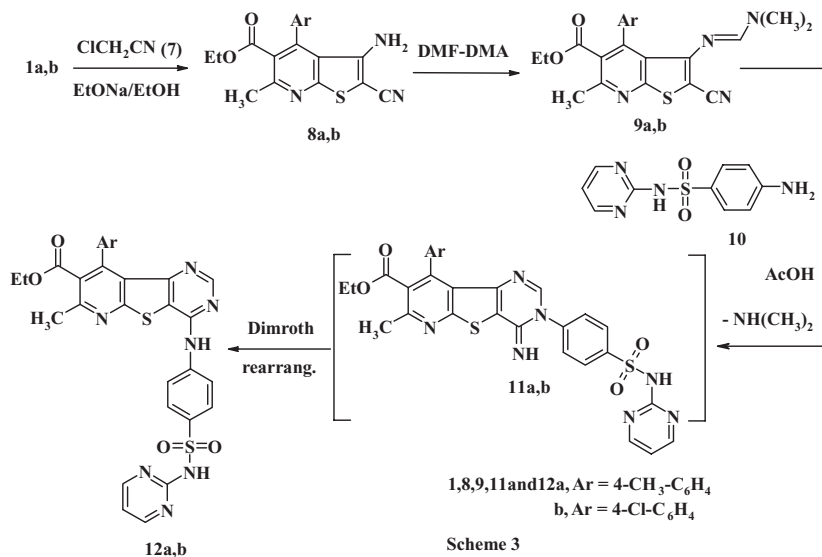
The reaction of **1a, b** with chloroacetonitrile (**7**) in sodium ethoxide solution under reflux afforded the corresponding ethyl 3-amino-2-cyanothieno[2,3-*b*]pyridine-5-carboxylate derivatives **8a, b**. The IR spectra of **8a, b** indicated the presence of the absorption band of NH₂ and CN group in addition to the ester carbonyl group. The ¹H NMR spectrum of **8a** revealed the NH₂ protons at $\delta = 5.46$ pm. Condensation of **8a, b** with DMF-DMA in dry dioxane under reflux yielded the ethyl 2-cyano-3-[(*N,N*-dimethylamino)methylene]amino}thieno[2,3-*b*]pyridine-5-carboxylate derivatives **9a, b**. The structure of **9a, b** was inferred via elemental analysis, spectral data, and chemical transformations (see Scheme 3 and the Experimental section).

The reaction of **9a, b** with sulfadiazine (**10**) in acetic acid under reflux gave the corresponding ethyl 4-[4-(aminosulfonyl)phenyl]amino]-7-methyl-9-arylpyrido[3',2':4,5]-thieno[3,2-*d*]-pyrimidine-8-carboxylate derivatives **12a, b**. The structures of **12a, b** were established based on elemental analysis and spectral studies (see Scheme 3 and the



Scheme 2

Experimental section). The IR spectra of **12a,b** showed the absorption bands of two NH groups, and their ^1H NMR spectra revealed the signals of two NH, pyrimidine protons, and absence of the signals of $\text{N}(\text{CH}_3)_2$ protons. The formation of **12a,b** in this reaction proceed via the addition of compound **10** to **9a,b** followed by cyclization with elimination



Scheme 3

Scheme 3

of dimethylamine, yielding the non-isolable intermediate imino compounds **11a,b**, which underwent Dimroth rearrangement^{41,43,50} under the applied reaction condition to give the final reaction products **12a,b**.

BIOLOGICAL ACTIVITY

Ten of the synthesized compounds were screened in vitro for their biological activities against four strains of bacteria (*Staphylococcus aureus*, *Bacillus cereus*, *Escherichia coli*, and *Pseudomonas aeruginosa*) by the agar diffusion technique.⁵¹ (see Table I S in the Supplemental Materials online).

EXPERIMENTAL

Melting points were measured with a Gallenkamp apparatus and are uncorrected. IR spectra in KBr discs were recorded on BRUKER Vector 22 FT-IR spectrophotometer. ¹H NMR spectra were determined in DMSO-d₆ at 300 MHz on Varian Mercury VX spectrometer using TMS as an internal standard. Chemical shifts are expressed as δ ppm and J as Hz units. Elemental analyses were carried out at the Microanalytical Center of Cairo University. Compounds **1a**,⁴⁷ **1b**,⁴⁹ and **2a,b**⁴⁸ were prepared according to the procedures in the literature.

Synthesis of Ethyl 6-[(2-[[4-(Aminosulfonyl)phenyl]amino]-2-oxoethylthio]-4-aryl-5-cyanonicotinate Derivatives **3a–d**

A solution of **1a,b** (0.01 mol) in DMF (20 mL) containing 0.03 mol of sodium acetate was treated with **2a,b** (0.01 mol). The reaction mixtures were stirred at room temperature for 2 h then poured onto ice-cold water. The precipitates that formed were collected by filtration and crystallized from the proper solvent to yield the reaction products **3a–d**, respectively (see Tables I and II).

Synthesis of Ethyl 3-Amino-2-([4-(aminosulfonyl)phenyl]amino)-carbonyl)-4-aryl-6-methylthieno[2,3-*b*]pyridine-5-carboxylate Derivatives **4a–d**

Method A (cyclization of **3a–d).** A solution of **3a–d** (0.01 mol) in ethanol (30 mL), containing 0.02 mol of potassium hydroxide, was heated under reflux for 3 h. The reaction mixture was then cooled, poured onto ice-cold water, and neutralized with dilute HCl (10%), and then the precipitated solid products were filtered off, washed with water, and crystallized from the proper solvent to yield the reaction products **4a–d** (see Tables I and II).

Method B (reaction of **1a,b with **2a,b**).** A solution of **1a,b** (0.01 mol) in ethanolic sodium ethoxide, prepared from 0.02 atom of sodium metal in 30 mL of ethanol, was treated with **2a,b** (0.01 mol) and then heated under reflux for 3 h. The reaction mixture was then cooled, poured onto ice-cold water, and neutralized with dilute HCl (10%). The solid products thus formed were filtered off and crystallized from the proper solvent to yield the reaction products **4a–d** (see Tables I and II).

Table I Characterization data of the newly synthesized compounds

Compound No.	Mp °C, Solvent	Yield % Color	Mol. Formula/ M. Wt.	Elemental analysis Calcd./Found %				
				C	H	N	S	Cl
3a	138–140	75	C ₂₅ H ₂₄ N ₄ O ₅ S ₂	57.24	4.61	10.68	12.22	—
	EtOH	Yellow	(524.62)	57.50	4.40	10.91	12.48	—
3b	140–142	72	C ₂₉ H ₂₆ N ₆ O ₅ S ₂	57.79	4.35	13.94	10.64	—
	EtOH	Yellow	(602.70)	57.99	4.08	13.68	10.35	—
3c	170–172	68	C ₂₄ H ₂₁ N ₄ O ₄ S ₂ Cl	52.89	3.88	10.28	11.77	6.50
	DMF	Yellow	(545.04)	52.60	3.60	10.56	11.51	6.30
3d	160–162	67	C ₂₈ H ₂₃ N ₆ O ₅ S ₂ Cl	53.97	3.72	13.49	10.29	5.69
	EtOH	Yellow	(623.11)	53.60	3.98	13.76	10.55	5.40
4a	260–262	71	C ₂₅ H ₂₄ N ₄ O ₅ S ₂	57.24	4.61	10.68	10.22	—
	Dioxane	Yellow	(524.62)	57.53	4.37	10.92	10.40	—
4b	269–271	65	C ₂₉ H ₂₆ N ₆ O ₅ S ₂	57.79	4.35	13.94	10.64	—
	Dioxane	Yellow	(602.70)	57.50	4.68	13.68	10.86	—
4c	296–298	70	C ₂₄ H ₂₁ N ₄ O ₅ S ₂ Cl	52.89	3.88	10.28	11.77	6.50
	DMF	Yellow	(545.04)	52.64	3.60	11.50	11.98	6.78
4d	254–256	61	C ₂₈ H ₂₃ N ₆ O ₅ S ₂ Cl	53.97	3.72	13.49	10.29	5.69
	Dioxane	Yellow	(623.11)	53.70	3.45	13.73	10.05	5.45
5a	313–315	65	C ₂₇ H ₂₄ N ₄ O ₅ S ₂	59.11	4.41	10.21	11.69	—
	DMF	White	(548.64)	59.40	4.20	10.45	11.46	—
5b	328–330	68	C ₃₁ H ₂₆ N ₆ O ₅ S ₂	59.41	4.18	13.41	10.23	—
	DMF	White	(626.72)	59.60	4.48	13.19	10.49	—
5c	230–232	67	C ₂₆ H ₂₁ N ₄ O ₅ S ₂ Cl	54.88	3.72	9.85	11.27	6.23
	EtOH	White	(569.06)	54.60	3.98	9.57	11.01	6.47
5d	270–272	58	C ₃₀ H ₂₃ N ₆ O ₅ S ₂ Cl	55.68	3.68	12.99	9.91	5.48
	AcOH	White	(647.14)	55.88	3.40	12.75	9.70	5.75
6a	286–288	64	C ₂₅ H ₂₁ N ₅ O ₅ S ₂	56.06	3.95	13.08	11.97	—
	DMF	Yellow	(535.60)	56.30	3.70	13.29	11.72	—
6b	282–284	53	C ₂₉ H ₂₃ N ₇ O ₅ S ₂	56.76	3.78	15.98	10.45	—
	AcOH	Yellow	(613.68)	56.56	3.50	15.77	10.74	—
6c	246–248	62	C ₂₄ H ₁₈ N ₅ O ₅ S ₂ Cl	51.84	3.26	12.26	11.53	6.38
	EtOH	Yellow	(556.02)	51.99	3.40	12.50	11.40	6.60
6d	280–282	60	C ₂₈ H ₂₀ N ₇ O ₅ S ₂ Cl	53.04	3.18	15.46	10.11	5.59
	AcOH	Yellow	(634.01)	53.30	3.50	15.70	10.33	5.81
8a	164–166	70	C ₁₉ H ₁₇ N ₃ O ₂ S	64.94	4.88	11.96	9.12	—
	EtOH	Yellow	(351.43)	64.70	4.61	11.72	9.34	—
8b	172–174	65	C ₁₈ H ₁₄ N ₃ O ₂ S Cl	58.14	3.79	11.30	8.62	3.79
	EtOH	Yellow	(371.85)	58.30	3.74	11.55	8.42	3.53
9a	146–148	75	C ₂₂ H ₂₂ N ₄ O ₂ S	65.00	5.46	13.78	7.89	—
	Dioxane	Yellow	(406.51)	65.26	5.70	13.90	7.61	—
9b	134–136	58	C ₂₁ H ₁₉ N ₄ O ₂ SCl	59.08	4.48	13.12	7.51	8.30
	EtOH	Yellow	(426.93)	59.23	4.70	13.51	7.74	8.58
12a	272–274	66	C ₃₀ H ₂₅ N ₇ O ₄ S ₂	58.91	4.12	16.03	10.48	—
	Dioxane	Yellow	(611.71)	58.70	4.40	16.31	10.68	—
12b	278–280	60	C ₂₉ H ₂₂ N ₇ O ₄ S ₂ Cl	55.10	3.51	15.51	10.14	5.61
	Dioxane	Yellow	(632.12)	55.30	3.30	15.80	10.38	5.35

Synthesis of Ethyl 3-[4-(aminosulfonyl)phenyl]-9-aryl-2,7-dimethyl-4-oxo-3,4-dihydropyrido[3',2':4,5]thieno[3,2-d]pyrimidine-8-carboxylate Derivatives 5a–d

A solution of the **4a–d** (0.01 mol) in glacial acetic acid (30 mL) was treated with acetic anhydride (5 mL) and then heated under reflux for 3 h. The reaction mixture was then

Table II Spectral data of the newly synthesized compounds

Compound No.	Spectral data, IR: ν (cm ⁻¹) and ¹ H NMR δ ppm
3a	IR: ν 3331, 3240 (NH ₂), 3120 (NH), 3030 (CH arom.), 2983 (CH aliph.), 2224 (CN), 1721, 1679 (2C=O). ¹ H NMR (DMSO-d ₆) δ 0.93 (t, J = 7.2 Hz, 3H, CH ₃), 2.35 (s, 3H, CH ₃), 2.56 (s, 3H, CH ₃), 4.09 (q, J = 7.2 Hz, 2H, CH ₂), 4.21 (s, 2H, SCH ₂), 7.13 (s, 2H, SO ₂ NH ₂), 7.33–7.79 (m, 8H, Ar–H) and 9.71 (s, 1H, NH).
3b	IR: ν 3343, 3105 (2NH), 30340 (CH arom.), 2980 (CH aliph.), 2223 (CN), 1722, 1690 (2C=O). ¹ H NMR (DMSO-d ₆) δ 0.98 (t, J = 7.2 Hz, 3H, CH ₃), 2.45 (s, 3H, CH ₃), 2.64 (s, 3H, CH ₃), 4.10 (q, J = 7.2 Hz, 2H, CH ₂), 4.26 (s, 2H, SCH ₂), 7.09 (t, J = 4.8 Hz, 1H, 5H-pyrimidine), 7.52–7.87 (m, 8H, Ar–H), 8.53 (d, J = 4.8 Hz, 2H, 4H- & 6H-pyrimidine), 9.95 (s, 1H, NH), 11.53 (br., 1H, NH).
3c	IR: ν 3270, 3226 (NH ₂), 3123 (NH), 3027 (CH aliph.), 2225 (CN), 1701, 1693 (2C=O). ¹ H NMR (DMSO-d ₆) δ 0.87 (t, J = 7.2 Hz, 3H, CH ₃), 2.49 (s, 3H, CH ₃), 3.97 (q, J = 7.2 Hz, 2H, CH ₂), 4.28 (s, 2H, SCH ₂), 7.24 (s, 2H, NH ₂), 7.42–7.77 (m, 8H, Ar–H), 10.69 (s, 1H, NH).
3d	IR: ν 3259, 3115 (2NH), 3045 (CH arom.), 2976 (CH aliph.), 2221 (CN), 1728, 1677 (2C=O). ¹ H NMR (DMSO-d ₆) δ 0.98 (t, J = 7.2 Hz, 3H, CH ₃), 2.39 (s, 3H, CH ₃), 4.0 (q, J = 7.2 Hz, 2H, CH ₂), 4.23 (s, 2H, SCH ₂), 7.08 (t, J = 4.8 Hz, 1H, 5H-pyrimidine), 7.32–7.84 (m, 8H, Ar–H), 8.59 (d, J = 4.8 Hz, 2H, 4H- & 6H-pyrimidine), 9.97 (s, 1H, NH) and 11.52 (br., 1H, NH).
4a	IR: ν 3474, 3362, 3329, 3225 (2NH ₂), 3110 (NH), 3048 (CH arom.), 2982 (CH aliph.), 1734, 1628 (2C=O). ¹ H NMR (DMSO-d ₆) δ 0.89 (t, J = 7.2 Hz, 3H, CH ₃), 2.41 (s, 3H, CH ₃), 2.60 (s, 3H, CH ₃), 3.97 (q, J = 7.2 Hz, 2H, CH ₂), 5.89 (s, 2H, NH ₂), 7.23 (s, 2H, SO ₂ NH ₂), 7.27–7.86 (m, 8H, Ar–H) and 9.81 (s, 1H, NH).
4b	IR: ν 3474, 3326 (NH ₂), 3220, 3104 (2NH), 3040 (CH arom.), 2958 (CH aliph.), 1720, 1638 (2C=O). ¹ H NMR (DMSO-d ₆) δ 0.89 (t, J = 7.2 Hz, 3H, CH ₃), 2.40 (s, 3H, CH ₃), 2.59 (s, 3H, CH ₃), 3.99 (q, J = 7.2 Hz, 2H, CH ₂), 5.89 (s, 2H, NH ₂), 7.03 (t, J = 4.8 Hz, 1H, 5H-pyrimidine), 7.42–7.77 (m, 8H, Ar–H), 8.49 (d, J = 4.8 Hz, 2H, 4H- & 6H-pyrimidine), 9.85 (s, 1H, NH), 11.60 (br., 1H, NH).
4c	IR: ν 3489, 3366, 3336, 3237 (2NH ₂), 3109 (NH), 3030 (CH arom.), 2982 (CH aliph.), 1740, 1626 (2C=O). ¹ H NMR (DMSO-d ₆) δ 0.1.02 (t, J = 7.2 Hz, 3H, CH ₃), 2.60 (s, 3H, CH ₃), 4.08 (q, J = 7.2 Hz, 2H, CH ₂), 5.56 (s, 2H, NH ₂), 7.15 (s, 2H, SO ₂ NH ₂), 7.37–7.76 (m, 8H, Ar–H) and 9.61 (s, 1H, NH).
4d	IR: ν 3478, 3313 (NH ₂), 3116 (NH), 3042 (CH arom.), 2958 (CH aliph.), 1722, 1636 (2C=O). ¹ H NMR (DMSO-d ₆) δ 0.91 (t, J = 7.4 Hz, 3H, CH ₃), 2.49 (s, 3H, CH ₃), 4.04 (q, J = 7.4 Hz, 2H, CH ₂), 5.89 (s, 2H, NH ₂), 7.02 (t, J = 4.8 Hz, 1H, 5H-pyrimidine), 7.42–7.94 (m, 8H, Ar–H), 8.49 (d, J = 4.8 Hz, 2H, 4H- & 6H-pyrimidine), 9.88 (s, 1H, NH) and 11.62 (br., 1H, NH).
5a	IR: ν 3487, 3326 (NH ₂), 3032 (CH arom.), 2978 (CH aliph.), 1731, 1682 (2C=O). ¹ H NMR (DMSO-d ₆) δ 0.99 (t, J = 7.2 Hz, 3H, CH ₃), 2.28 (s, 3H, CH ₃), 2.40 (s, 3H, CH ₃), 2.65 (s, 3H, CH ₃), 4.02 (q, J = 7.2 Hz, 2H, CH ₂), 7.13 (s, 2H, SO ₂ NH ₂), 7.37–7.84 (m, 8H, Ar–H).
5b	IR: ν 3361 (NH), 3035 (CH arom.), 2983 (CH aliph.), 1721, 1671 (2C=O). ¹ H NMR (DMSO-d ₆) δ 0.96 (t, J = 7.2 Hz, 3H, CH ₃), 2.35 (s, 3H, CH ₃), 2.43 (s, 3H, CH ₃), 2.69 (s, 3H, CH ₃), 4.05 (q, J = 7.2 Hz, 2H, CH ₂), 7.10 (t, J = 4.8 Hz, 1H, 5H-pyrimidinyl), 7.42–7.76 (m, 8H, Ar–H), 8.50 (d, J = 4.8 Hz, 2H, 4H- & 6H-pyrimidinyl) and 11.28 (br., 1H, NH).
5c	IR: ν 3449, 3345 (NH ₂), 3041 (CH arom.), 2979 (CH aliph.) 1726, 1678 (2C=O). ¹ H NMR (DMSO-d ₆) δ = 0.97 (t, J = 7.4 Hz, 3H, CH ₃), 1.86 (s, 3H, CH ₃), 2.69 (s, 3H, CH ₃), 4.01 (q, J = 7.4 Hz, 2H, CH ₂), 7.37 (s, 2H, SO ₂ NH ₂), 7.41–8.09 (m, 8H, Ar–H).
5d	IR: ν 3374 (NH), 3025 (CH arom.), 2977 (CH aliph.), 1733, 1691 (2C=O). ¹ H NMR (DMSO-d ₆) δ 0.98 (t, J = 7.2 Hz, 3H, CH ₃), 2.39 (s, 3H, CH ₃), 2.61 (s, 3H, CH ₃), 4.09 (q, J = 7.2 Hz, 2H, CH ₂), 7.09 (t, J = 4.8 Hz, 1H, 5H-pyrimidinyl), 7.35–7.89 (m, 8H, Ar–H), 8.58 (d, J = 4.8 Hz, 2H, 4H- & 6H-pyrimidinyl) and 11.48 (br., 1H, NH).
6a	IR: ν 3313, 3223 (NH ₂) 3015 (CH arom.), 2972 (CH aliph.), 1728, 1659 (2C=O). ¹ H NMR (DMSO-d ₆) δ 1.02 (t, J = 7.2 Hz, 3H, CH ₃), 2.37 (s, 3H, CH ₃), 2.46 (s, 3H, CH ₃), 4.12 (q, J = 7.2 Hz, 2H, CH ₂), 7.20 (s, 2H, SO ₂ NH ₂), 7.45–7.94 (m, 8H, Ar–H).

(Continued on next page)

Table III Spectral data of the newly synthesized compounds (*Continued*)

Compound No.	Spectral data, IR: ν (cm ⁻¹) and ¹ H NMR δ ppm
6b	IR: ν 3110 (NH), 3040 (CH arom.), 2940 (CH aliph.), 1720, 1680 (2 C=O). ¹ H NMR (DMSO-d ₆) δ 0.93 (t, J = 7.2 Hz, 3H, CH ₃), 2.39 (s, 3H, CH ₃), 2.72 (s, 3H, CH ₃), 4.04 (q, J = 7.2 Hz, 2H, CH ₂), 7.04 (t, J = 4.8 Hz, 1H, 5H-pyrimidine), 7.31–8.17 (m, 8H, Ar–H), 8.51 (d, J = 4.8 Hz, 2H, 4H- & 5H-pyrimidine), 12.10 (br., 1H, NH).
6c	IR: ν 3310, 3223 (NH ₂), 3015 (CH arom.), 2976 (CH aliph.), 1728, 1675 (2C=O). ¹ H NMR (DMSO-d ₆) δ 1.05 (t, J = 7.2 Hz, 3H, CH ₃), 2.41 (s, 3H, CH ₃), 4.10 (q, J = 7.2 Hz, 2H, CH ₂), 7.19 (s, 2H, SO ₂ NH ₂), 7.53–7.88 (m, 8H, Ar–H).
6d	IR: ν 3364 (NH), 3031 (CH arom.), 2983 (CH aliph.), 1725, 1675 (2 C=O). ¹ H NMR (DMSO-d ₆) δ 0.97 (t, J = 7.2 Hz, 3H, CH ₃), 2.61 (s, 3H, CH ₃), 4.09 (q, J = 7.2 Hz, 2H, CH ₂), 7.14 (t, J = 4.8 Hz, 1H, 5H-pyrimidine), 7.40–8.09 (m, 8H, Ar–H), 8.58 (d, J = 4.8 Hz, 2H, 4H- & 5H-pyrimidine), 11.91 (br., 1H, NH).
8a	IR: ν 3463, 3335 (NH ₂), 3040 (CH arom.), 2979 (CH aliph.), 2198 (CN), 1727 (C=O). ¹ H NMR (DMSO-d ₆) δ 0.88 (t, J = 7.2 Hz, 3H, CH ₃), 2.41 (s, 3H, CH ₃), 2.58 (s, 3H, CH ₃), 3.97 (q, J = 7.2 Hz, 2H, CH ₂), 5.46 (s, 2H, NH ₂), 7.27 (d, J = 8.4 Hz, 2H, Ar–H) and 7.37 (d, J = 8.1 Hz, 2H, Ar–H).
8b	IR: ν 3483, 3342 (NH ₂), 3035 (CH arom.), 2977 (CH aliph.), 2198 (CN), 1728 (C=O). ¹ H NMR (DMSO-d ₆) δ 0.94 (t, J = 7.2 Hz, 3H, CH ₃), 2.67 (s, 3H, CH ₃), 4.04 (q, J = 7.2 Hz, 2H, CH ₂), 5.33 (s, 2H, NH ₂), 7.36 (d, J = 8.4 Hz, 2H, Ar–H) and 7.45 (d, J = 8.1 Hz, 2H, Ar–H).
9a	IR: ν 3035 (CH arom.), 2972 (CH aliph.), 2202 (CN), 1729 (C=O). ¹ H NMR (DMSO-d ₆) δ 0.86 (t, J = 7.2 Hz, 3H, CH ₃), 2.30 (s, 3H, CH ₃), 2.36 (s, 3H, CH ₃), 2.69 (s, 3H, CH ₃), 2.79 (s, 3H, CH ₃), 3.98 (q, J = 7.2 Hz, 2H, CH ₂), 7.01 (d, J = 8.1 Hz, 2H, Ar–H), 7.17 (d, J = 8.1 Hz, 2H, Ar–H) and 7.49 (s, 1H, N = CH).
9b	IR: ν 3483, 3342 (NH ₂), 3035 (CH arom.), 2977 (CH aliph.), 2198 (CN), 1728 (C=O). ¹ H NMR (DMSO-d ₆) δ 0.90 (t, J = 7.2 Hz, 3H, CH ₃), 2.35 (s, 3H, CH ₃), 2.76 (s, 3H, CH ₃), 2.86 (s, 3H, CH ₃), 4.01 (q, J = 7.2 Hz, 2H, CH ₂), 7.18 (d, J = 8.1 Hz, 2H, Ar–H), 7.44 (d, J = 8.1 Hz, 2H, Ar–H) and 7.59 (s, 1H, N = CH).
12a	IR: ν 3307, 3121 (2NH), 3051 (CH arom.), 2975 (CH aliph.), 1725 (C=O). ¹ H NMR (DMSO-d ₆) δ = 0.97 (t, J = 7.2 Hz, 3H, CH ₃), 2.45 (s, 3H, CH ₃), 2.76 (s, 3H, CH ₃), 4.00 (q, J = 7.2 Hz, 2H, CH ₂), 7.10 (t, J = 4.8 Hz, 1H, 5H-pyrimidinyl), 7.22–7.82 (m, 8H, Ar–H), 8.55 (s, 1H, C2-H-pyrimidine) 8.48 (d, J = 4.8 Hz, 2H, 4H- and 6H-pyrimidinyl), 9.82 (s, 1H, NH) and 11.25 (br., 1H, NH).
12b	IR: ν 3321, 3112 (NH), 3045 (CH-arom), 2987 (CH aliph.), 1717 (CO). ¹ H NMR (DMSO-d ₆) δ = 1.06 (t, J = 7.2 Hz, 3H, CH ₃), 2.66 (s, 3H, CH ₃), 4.11 (q, J = 7.2 Hz, 2H, CH ₂), 7.14 (t, J = 4.8 Hz, 1H, 5H-pyrimidinyl), 7.31–7.88 (m, 8H, Ar–H), 8.49 (s, 1H, C2-H-pyrimidine) 8.55 (d, J = 4.8 Hz, 2H, 4H- and 6H-pyrimidinyl), 9.72 (s, 1H, NH) and 11.31 (br., 1H, NH).

cooled. The solid products thus formed were filtered off and crystallized from the proper solvent to yield the reaction products **5a–d** (see Tables I and II).

Synthesis of Ethyl 3-[4-(aminosulfonyl)phenyl]-9-aryl-7-methyl-4-oxo-3,4-dihydropyrido[3',2':4,5]thieno[3,2-d][1,2,3]triazine-8-carboxylate Derivatives **6a–d**

A solution of **4a–d** (0.01 mol) in glacial acetic acid (30 mL) was treated with cold solution of sodium nitrite (0.02 mol in 3 mL of water), and the reaction mixture was stirred in an ice chest for 2 h. The solid products thus formed were filtered off and crystallized from the proper solvent to yield the reaction products **6a–d** (see Tables I and II).

Synthesis of Ethyl 3-Amino-2-cyano-6-methyl-4-arylthieno[2,3-*b*]-pyridine-5-carboxylate Derivatives **8a,b**

A solution of **1a,b** (0.01 mol) in ethanolic sodium ethoxide, prepared from 0.02 atom of sodium metal in 30 mL of ethanol, was treated with chloroacetonitrile (**7**) (0.01 mol) and then heated under reflux for 3 h. The reaction mixture was then cooled, poured onto ice-cold water, and neutralized with dilute HCl (10%). The solid products thus formed were filtered off and crystallized from ethanol to yield the reaction products **8a,b** (see Tables I and II).

Synthesis of Ethyl 2-Cyano-3-[(*N,N*-dimethylamino)-methylene]amino]thieno[2,3-*b*]pyridine-5-carboxylate Derivatives **9a,b**

A solution of the appropriate **8a,b** (0.01 mol) in dry xylene (30 mL) and DMF-DMA (0.015 mol) was heated under reflux for 4 h. The reaction mixture was then cooled. The solid products thus formed were filtered off and crystallized from the proper solvent to yield the reaction products **9a,b** (see Tables I and II).

Synthesis of Ethyl 4-{[4-(Aminosulfonyl)phenyl]amino}-7-methyl-9-arylpseudo[3',2':4,5]thieno[3,2-*d*]pyrimidine-8-carboxylate Derivatives **12a,b**

A solution of the appropriate formamidine derivatives **9a,b** (0.01 mol) and sulfadiazine (**10**) (0.01 mol) in glacial acetic acid (30 mL) was heated under reflux for 3–5 h. The reaction mixture was then cooled. The solid products thus formed were filtered off and crystallized from dioxane to yield the products **12a,b** (see Tables I and II).

REFERENCES

1. Y. Funahashi, N. H. Sugi, T. Semba, Y. Yamamoto, S. Hamaoka, N. Tsukahara-Tamai, Y. Ozawa, A. Tsuruoka, K. Nara, K. Takahashi, T. Okabe, J. Kamata, T. Owa, N. Ueda, T. Haneda, M. Yonaga, K. Yoshimatsu, and T. Wakabayashi, *Cancer Res.*, **62**, 6116 (2002).
2. P. L. Wash, T. Z. Hoffman, B. M. Wiley, C. Bonnefous, N. D. Smith, M. S. Sertic, C. M. Lawrence, K. T. Symons, P. Nguyen, K. D. Lustig, X. Guo, T. Annable, S. A. Noble, J. H. Hager, C. A. Hassig, and J. W. Malecha, *Bioorg. Med. Chem. Lett.*, **18**, 6482 (2008).
3. (a) J. Sławiński and M. Gdaniec, *Eur. J. Med. Chem.*, **40**(4), 377 (2005); (b) T. Semba, Y. Funahashi, N. Ono, Y. Yamamoto, N. H. Sugi, M. Asada, K. Yoshimatsu, and T. Wakabayashi, *Clin. Cancer Res.*, **10**, 1430 (2004).
4. (a) Q. Chen, P. N. P. Rao, and E. E. Knaus, *Bioorg. Med. Chem.*, **13**(7), 2459 (2005); (b) Q. Chen, P. N. P. Rao, and E. E. Knaus, *Bioorg. Med. Chem.*, **13**(15), 4694 (2005).
5. Md. J. Uddin, P. N. P. Rao, and E. E. Knaus, *Bioorg. Med. Chem.*, **13**(2), 417 (2005).
6. H. Moreno-Díaz, R. Villalobos-Molina, R. Ortiz-Andrade, D. Díaz-Coutiño, J. L. Medina-Franco, S. P. Webster, M. Binnie, S. Estrada-Soto, M. Ibarra-Barajas, I. León-Rivera, and G. Navarrete-Vázquez, *Bioorg. Med. Chem. Lett.*, **18**(9), 2871 (2008).
7. A. K. Gadad, M. N. Noolyi, and R. V. Karpoomath, *Bioorg. Med. Chem.*, **12**(21), 5651 (2004).
8. V. K. Agrawal, S. Bano, C. T. Supuran, and P. V. Khadikar, *Eur. J. Med. Chem.*, **39**(7), 593 (2004).
9. (a) N. Masuda, O. Yamamoto, M. Fujii, T. Ohgami, J. Fujiyasu, T. Kontani, A. Moritomo, M. Orita, H. Kurihara, H. Koga, S. Kageyama, M. Ohta, H. Inoue, T. Hatta, M. Shintani, H. Suzuki, K. Sudo, Y. Shimizu, E. Kodama, M. Matsuoka, M. Fujiwara, T. Yokota, S. Shigeta, and M.

- Baba, *Bioorg. Med. Chem.*, **13**(4), 949 (2005); (b) C. M. Yeung, L. L. Klein, C. A. Flentge, J. T. Randolph, C. Zhao, M. Sun, T. Dekhtyar, V. S. Stoll, and D. J. Kempf, *Bioorg. Med. Chem. Lett.*, **15**, 2275 (2005).
10. A. Y. Kovalevsky, J. M. Louis, A. Aniana, A. K. Ghosh, and I. T. Weber, *J. Mol. Biol.*, **384**, 178 (2008).
 11. (a) R. Villar, I. Encío, M. Migliaccio, Mj. Gil, and V. Martinez-Merino, *Bioorg. Med. Chem.*, **12**, 963 (2004); (b) I. Encío, Dj. Morré, R. Villar, Mj. Gil, and V. Martínez-Merino, *Br. J. Cancer*, **92**, 690 (2005).
 12. N. Kaur, A. Kaur, Y. Bansal, D. I. Shah, G. Bansal, and M. Singh, *Bioorg. Med. Chem.*, **16**, 10210 (2008).
 13. (a) Y. A. Ammar, N. M. Saleh, J. A. Micky, H. A. S. Abbas, and M. S. A. El-Gaby, *Indian J. Chem.*, **43B**, 2203 (2004); (b) S. J. Kim, M. H. Jung, K. H. Yoo, J. Cho, and C. Oh, *Bioorg. Med. Chem. Lett.*, **18**, 5815 (2008); (c) M. J. Nieta, F. L. Alovero, R. H. Manzo, and M. R. Mazzieri, *Eur. J. Med. Chem.*, **40**(4), 361 (2005).
 14. J. N. Domínguez, C. León, J. Rodrigues, N. G. de Domínguez, J. Gut, and P. J. Rosethal, *Il Farmaco*, **60**, 307 (2005).
 15. M. Anderson, D. M. Andrews, A. J. Barker, C. A. Brassington, J. Breed, K. F. Byth, J. D. Culshaw, M. R. V. Finlay, E. Fisher, H. H. J. McMiken, C. P. Green, D. W. Heaton, I. A. Nash, N. J. Newcombe, S. E. Oakes, R. A. Pauptit, A. Roberts, J. J. Stanway, A. P. Thomas, J. A. Tucker, M. Walker, and H. M. Weir, *Bioorg. Med. Chem. Lett.*, **18**, 5487 (2008).
 16. A. Krauze, S. Germame, O. Eberlins, I. Sturms, V. Klusa, and G. Duburs, *Eur. J. Med. Chem.*, **34**, 301 (1999).
 17. A. Krause, L. Baumann, L. Sile, M. Vilums, L. Cernova, R. Vitolina, G. Duburs, and J. Stradinš, *Chem. Heterocycl. Compd.*, **40**(7), 876 (2004).
 18. A. E. Abdel-Rahman, E. A. Bakhite, and E. A. Al-Taifi, *Pharmazie*, **58**(6), 372 (2003).
 19. U. Rosentreter, T. Kraemer, A. Vaupel, W. Huebsch, N. Diedrichs, T. Krahn, K. Dembowski, and P. J. Stasch, PCT Int. Appl. WO, 02 70, 485 (2002); *Chem. Abstr.*, **137**, 216880g (2002).
 20. D. G. Croshy, R. W. Emerson, T. C. Miller, D. P. Peterson, and L. P. Sharap, PCT Int. Appl. WO 01 19, 185, (2001); *Chem. Abstr.*, **134**, 218309, (2001).
 21. B. Krislin and H. Andreas, *Bioorg. Med. Chem. Lett.*, **12**(3), 411, (2002).
 22. (a) M. E. Schnute, M. M. Cudaly, R. J. Brideau, F. L. Homa, T. A. Hopkins, M. L. Knechtel, N. L. Oien, T. W. Pitts, R. A. Poorman, M. W. Wathen, and J. L. Wieber, *J. Med. Chem.*, **48**(18), 5794 (2005); (b) M. E. Schnute, D. J. Anderson, R. J. Brideau, F. L. Ciske, S. A. Collier, M. M. Cudahy, M. Eggen, M. J. Genin, T. A. Hopkins, T. M. Judge, E. J. Kim, M. L. Knechtel, S. K. Nair, J. A. Nieman, N. L. Oien, A. Scott, S. P. Tanis, V. A. Vaillancourt, M. W. Wathen, and J. L. Wieber, *Bioorg. Med. Chem. Lett.*, **17**, 3349 (2007).
 23. (a) F. A. Attaby, A. H. H. Elghandour, M. A. Ali, and Y. M. Ibrahim, *Phosphorous, Sulfur, and Silicon*, **182**, 695 (2007); (b) F. A. Attaby, M. A. Ali, A. H. H. Elghandour and Y. M. Ibrahim, *Phosphorous, Sulfur, and Silicon*, **181**, 1 (2006).
 24. R. H. Bahekar, M. R. Jain, P. A. Jadav, V. M. Prajapati, D. N. Patel, A. A. Gupta, A. Sharma, R. Tom, D. Bandyopadhyaya, H. Modi, and P. R. Patel, *Bioorg. Med. Chem.*, **15**, 6782 (2007).
 25. S. M. Eldin, *Z. Naturforsch.*, **4b**, 674 (1999).
 26. A. M. Hussin, F. A. Abu-Shanab, and E. A. Ishak, *Phosphorous, Sulfur, and Silicon*, **159**, 55 (2000).
 27. G. P. Moloney, *Molecules*, **6**, M203 (2001).
 28. I. Hayakawa, R. Shioya, T. Agatsuma, H. Furukawa, and Y. Sugano, *Bioorg. Med. Chem. Lett.*, **14**, 3411 (2004).
 29. A. M. R. Bernardino, L. C. da S. Pinheiro, C. R. Rodrigues, N. I. Loureiro, H. C. Castro, A. Lanfredi-Rangel, J. Sabtini-Lopes, J. C. Borges, J. M. Carvalho, G. A. Romeiro, V. F. Ferreira, I. C. P. P. Fruguphetti, and M. A. Vannier-Santos, *Bioorg. Med. Chem.*, **14**, 5765 (2006).
 30. J. M. Quintela, C. Peinador, C. Veiga, L. Gonzales, L. M. Botana, A. Alfonso, and R. Riguera, *Bioorg. Med. Chem.*, **6**, 1911 (1998).

31. J. M. Quintela, C. Peinador, L. Gonzales, R. Iglesias, A. Parama, F. Alvares, M. L. Sanmartin, and R. Riguera, *Eur. J. Med. Chem.*, **38**, 265 (2003).
32. (a) G. Wagner, S. Leistner, H. Vieweg, U. Krasselt, and J. Prantzt, *Pharmazie*, **48**, 342 (1993); (b) N. Boehm, U. Krasselt, S. Leistner, and G. Wagner, *Pharmazie*, **47**, 897 (1992).
33. A. Paramá, R. Iglesias, F. Álvarez, J. M. Lerio, J. M. Quntela, C. Peinador, L. González, R. Riguera, and M. L. Sanmartín, *Dis. Aquat. Organ.*, **62**, 97 (2004).
34. E. G. Paronikyan, A. S. Noravyan, Sh. F. Akopyan, F. G. Arsenyan, G. M. Stepanyan, and B. T. Garibdzhanyan, *Pharma. Chem. J.*, **40**(6), 3 (2006).
35. B. Martínez-Poveda, R. Muñoz-Chápuli, S. Rodríguez-Nieto, J. M. Quintela, A. Fernández, M. Medina, and A. R. Quesada, *Mol. Cancer Ther.*, **6**(10), 2675 (2007).
36. J. M. Quintela, C. Peinador, I. M. González, R. Riguera, I. Rioja, M. C. Terencio, A. Ubeda, and M. J. Alcaraz, *J. Med. Chem.*, **42**(22), 4720 (1999).
37. M. S. A. El-Gaby, A. M. Sh. El-Sharief, A. A. Atalla, and A. A. A. M. El-Adasy, *J. Chin. Chem. Soc.*, **51**(2), 327 (2004).
38. M. A. M. Gad-Elkareem, *Afinidad*, **63**(523), 247 (2006).
39. G. G. Mohamed and M. A. M. Gad-Elkareem, *Spectrochim. Acta A*, **68**(5), 1382 (2007).
40. A. M. Hussein, A. A. M. El-Adasy, M. A. M. Gad-Elkareem, and I. M. Othman, *Organic Chemistry, an Indian Journal, OCAIJ*, **4**(3), 178 (2008).
41. M. A. M. Gad-Elkareem, A. M. Abdel-Fattah, and M. A. A. Elneairy, *Phosphorous, Sulfur, and Silicon*, **181**(2), 891 (2006).
42. M. A. A. Elneairy, M. A. M. Gad-Elkareem, and A. M. Taha, *J. Sulfur Chem.*, **26**(4–5), 381 (2005).
43. M. A. M. Gad-Elkareem, M. A. A. Elneairy, and A. M. Taha, *Heteroatom Chem.*, **18**(4), 405 (2007).
44. M. A. A. Elneairy, M. A. M. Gad-Elkareem, and A. M. Taha, *Heteroatom Chem.*, **18**(4), 399 (2007).
45. M. A. M. Gad-Elkareem, A. M. Abdel-Fattah, and M. A. A. Elneairy, *Can. J. Chem.*, **85**, 592 (2007).
46. T. I. El-Emary, A. Khalil, G. A. M. El-Hag Ali, and A. A. A. M. El-Adasy, *Phosphorous, Sulfur, and Silicon*, **180**, 19 (2005).
47. V. A. Artenov, L. A. Rodinveskaya, A. M. Schestopalov, and V. P. Litvonov, *Kim. Geterstsikel Soedin*, 122 (1994); *Chem. Abstr.*, **122**, 31630x (1995).
48. U. P. Basu and J. Sikdar, *J. Ind. Chem. Soc.*, 466 (1947).
49. F. A. Attaby, L. I. Ibrahim, S. M. Eldin, and A. K. K. El-Louh, *Phosphorous, Sulfur, and Silicon*, **73**, 127 (1992).
50. V. A. Markarov, O. B. Ryabova, L. M. Alekseeva, A. S. Shashkov, and V. G. Granik, *Chem. Heterocycl. Compd.*, **39**(2), 238 (2003).
51. L. P. Carrod and F. D. Grady, *Antibiotics and Chemotherapy*, 3rd ed. (Churchill Livingstone, Edinburgh, UK, 1972), p. 477.