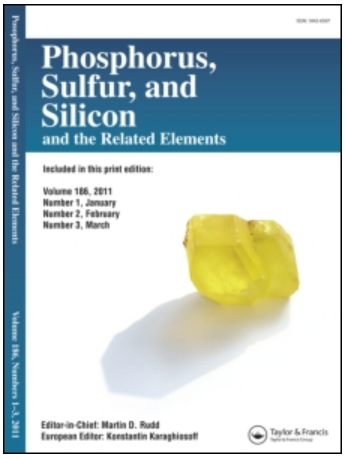

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Synthesis, Characterization, and Reactions of Pyridine-3-Carbonitrile Derivatives

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Synthesis, Characterization, and Reactions of Pyridine-3-Carbonitrile Derivatives

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*2-Thioxopyridine-3-carbonitrile derivatives **6a-c** reacted with several halogen containing reagents **7a-d** to afford the corresponding thieno[2,3-b]pyridine derivatives **9a-l,** respectively. Thieno[2,3-b]pyridines **9c, g,k** used for the preparation of their corresponding carbohydrazide derivatives **10a-c** which in turn, used as good synthons for the synthesis of N-phenylmethylenethieno[2,3-b]pyridine-2-carbohydrazides **13**a–c, pyrido[3′,2′:4,5]thieno[3,2-d]pyrimidinones **15a-c**, **16a-c** and **17** and 1,3,4-oxadiazole-2-thiols **20a-c** and **21a-c** via their reactions with benzaldehyde or benzylidenemalononitrile, triethylorthoformate and carbon disulfide followed by hydrazine hydrate respectively. Considering the data of IR, ^{1}H NMR, mass spectra, and elemental analyses elucidated the chemical structures of the newly synthesized heterocyclic compounds.*

Keywords 1,3,4-oxadiazole-2-thiols; 2-Cyanoethanethioamide; 2-thioxopyridine-3-carbonitrile; carbohydrazides; pyridothienopyrimidinones; thieno[2,3-b]pyridine; thiopyranopyridines triethyl orthoformate

INTRODUCTION

Synthetic potentiality, as well as the reported biological activity of 2-thioxopyridine,[1–3] thieno[2,3-b]pyridine,[4,5] and pyridothienopyrimidines[6,7] stimulated our interest to synthesize and characterize several derivatives of these ring systems required for several chemical transformation as well as medicinal chemistry programs and this target represents a continuation of our previous work.[8–31] In this article, we are interested in the synthesis of 2-thioxo-1,2-dihydropyridine-3-carbonitrile derivatives **6a–c**, as well as to investigate their synthetic potentiality with several reagents to achieve our target.

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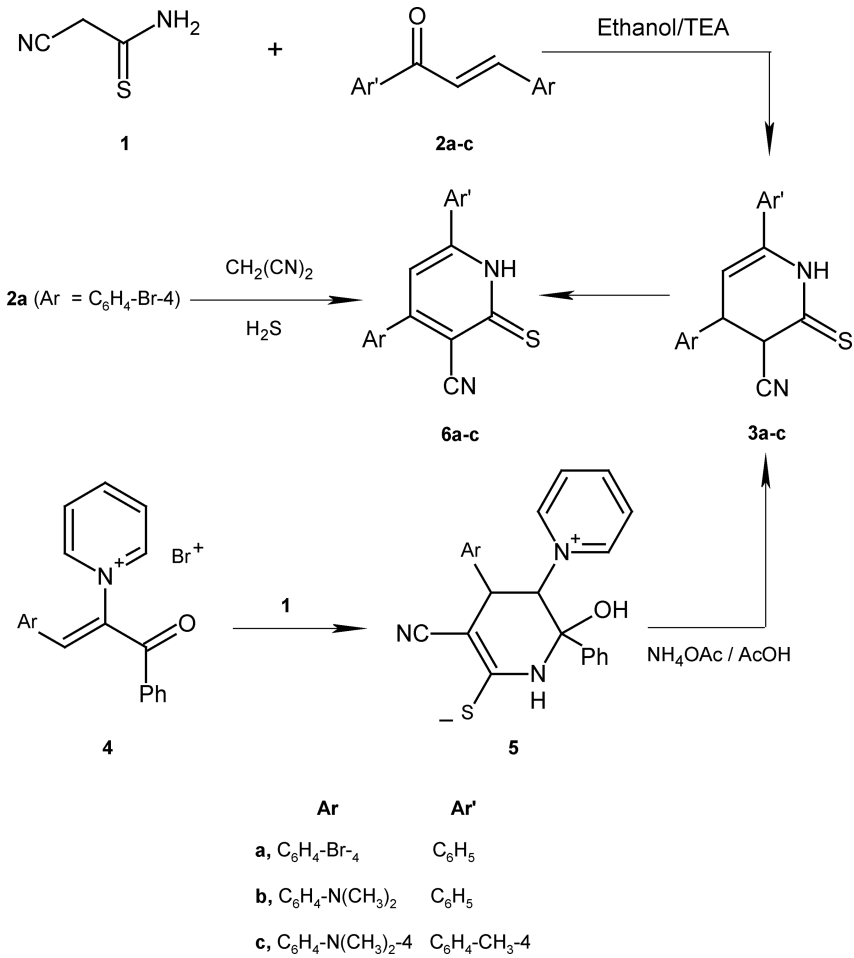
RESULTS AND DISCUSSION

4-(4-bromophenyl)-6-phenyl-2-thioxo-1,2-dihydropyridine-3-carbonitrile**(6a)** synthesized either by the reaction 3-(4-bromophenyl)-1-phenylprop-2-en-1-one (**2a**) with malononitrile/H_2S[32–34] or by the reaction of pyridinium bromide **4** with 2-cyanoethanethioamide (**1**) followed by ammonium acetate.[35] On carrying out such reactions, compound **6a** was obtained in a very low yield and in an impure state, and this stimulate our interest to synthesize **6a** via another pathway. Thus, it has been found that **1** reacted with 3-(4-bromophenyl)-1-phenylprop-2-en-1-one **(2a)** in ethanol containing the catalytic amount of triethyl amine gave 4-(4-bromophenyl)-6-phenyl-2-thioxo-1,2-dihydropyridine-3-carbonitrile **6a**. The formation of **6a** seemed to be proceeded via the addition of $–CH_2-$ in **1** on the –CH=CH- in **2a** followed by spontaneous cyclization to **3a** which auto-oxidizes under the reaction conditions to afford **6a** in good yield and in very pure state.

Similarly, **1** reacted with each of 3-[4-(dimethylamino)phenyl]-1-phenylprop-2-en-1-one (**2b**) and 3-[4-(dimethylamino)phenyl]-1-(4-methylphenyl)prop-2-en-1-one (**2c**) under the same experimental conditions to afford the corresponding **6b**,**c** respectively. The chemical structure of **6a-c** was elucidated based on its IR, ^{1}H NMR, and its elemental analyses (cf. Experimental section). Moreover, the mass spectrum of **6b** as a typical example gave m/z = 331, which corresponds to the molecular weight of the molecular formula $C_{20}H_{17}N_3S$ of the assigned structure. Also, such mass spectrum gave several peaks with their fragments and this confirms the given structure (cf. Chart 1 and Experimental section).

Synthons **6a–c** used as good starting materials for the present study, thus, it has been found that **6a** reacted with 1-chloroacetone **(7a)** 1:1 in methanolic sodium methoxide solution via the dehydrochlorination followed by addition of $-CH_2-$ on the CN group to afford the imino derivative **(I)**, which spontaneously rearranged to give a reaction product **9a**. Similarly, compounds **9e**,**i** obtained via the reaction of **6b**,**c** with **7a** under the same above mentioned experimental conditions. The IR (cm^{-1}) spectra of these reaction products showed no bands of the CN function, and instead, the newly formed NH_2 group was detected; thus, we can conclude that both CN and $–SCH_2-$ were involved in cyclization step to afford directly **9a**,**e**,**i**. Also, compounds **6a-c** reacted with each of 2-chloroacetamide, ethyl chloroacetate and 2-bromo-1-(4-chlorophenyl)-ethanone **7b–d** under the same above mentioned experimental conditions to afford the corresponding thieno[2,3-b]pyridine derivatives **9b–d**, **g**,**h**,**l** and **8f**,**j**,**k** whose structures established by considering the data of IR, ^{1}H NMR and elemental analyses (cf. Experimental section and Chart 2). Further confirmation of **8f**,**j**,**k** structures

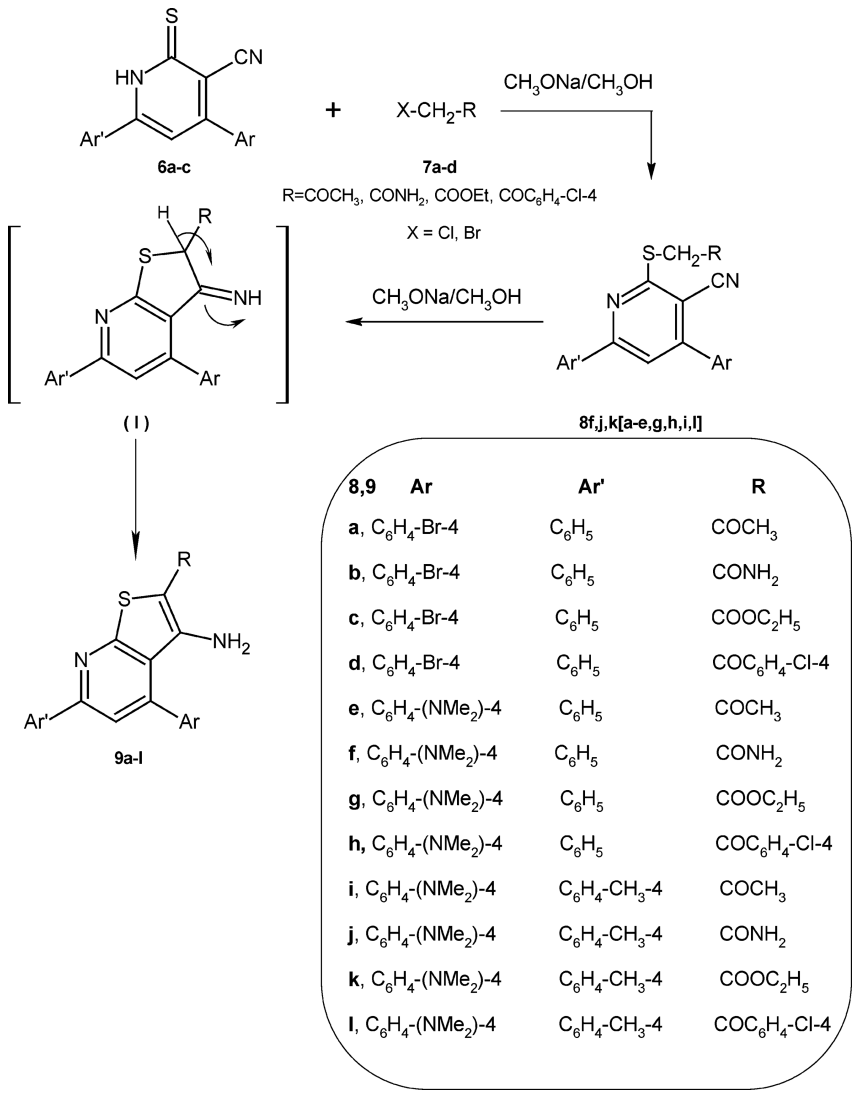


Ar	Ar'
a, C_6H_4-Br-$_4$	C_6H_5
b, C_6H_4-N$(CH_3)_2$	C_6H_5
c, C_6H_4-N$(CH_3)_2$-4	C_6H_4-CH_3-4

CHART 1

was given through their cyclization in methanolic sodium methoxide to afford the corresponding thieno[2,3-b]pyridine derivatives **9f**,**j**,**k** respectively.

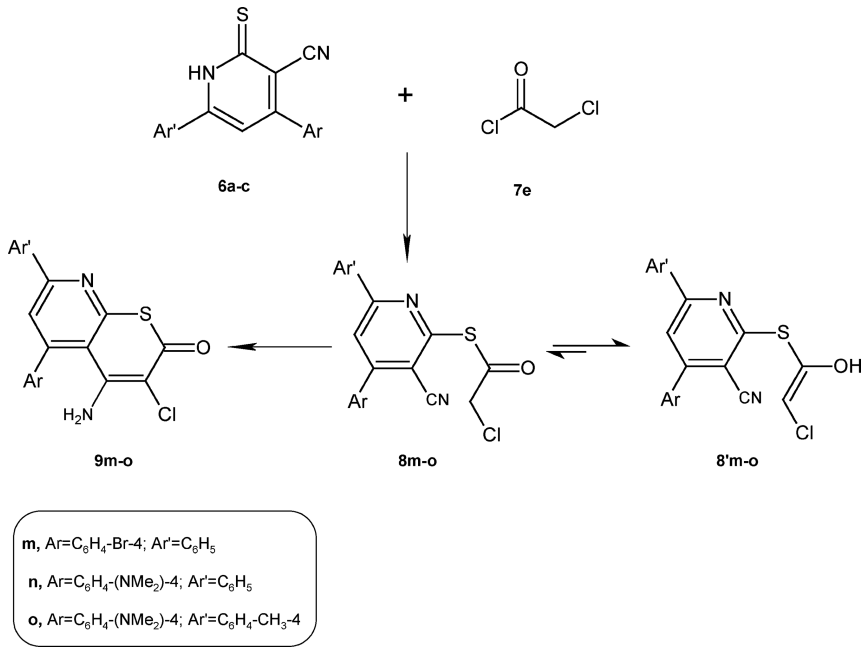
On the other hand, compound **6a** reacted with chloroacetyl chloride **7e** under the same above-mentioned experimental conditions to afford the corresponding S-4-(4-bromophenyl)-3-cyano-6-phenyl-pyridin-2-yl-2-chloroethanethioate **8m**, which converted to its enol form 2-(2-chloro-1-hydroxyvinylthio)-4-(4-bromophenyl)-6-phenyl-pyridine-3-nitrile **(8′m)**. The reaction seemed to proceed via the dehydrochlorination between **6a** and **7e** selectively along



8,9 Ar	Ar'	R
a, C_6H_4-Br-4	C_6H_5	$COCH_3$
b, C_6H_4-Br-4	C_6H_5	$CONH_2$
c, C_6H_4-Br-4	C_6H_5	$COOC_2H_5$
d, C_6H_4-Br-4	C_6H_5	COC_6H_4-Cl-4
e, C_6H_4-(NMe_2)-4	C_6H_5	$COCH_3$
f, C_6H_4-(NMe_2)-4	C_6H_5	$CONH_2$
g, C_6H_4-(NMe_2)-4	C_6H_5	$COOC_2H_5$
h, C_6H_4-(NMe_2)-4	C_6H_5	COC_6H_4-Cl-4
i, C_6H_4-(NMe_2)-4	C_6H_4-CH_3-4	$COCH_3$
j, C_6H_4-(NMe_2)-4	C_6H_4-CH_3-4	$CONH_2$
k, C_6H_4-(NMe_2)-4	C_6H_4-CH_3-4	$COOC_2H_5$
l, C_6H_4-(NMe_2)-4	C_6H_4-CH_3-4	COC_6H_4-Cl-4

CHART 2

the more electrophilic C-atom (ClCO- not $ClCH_2$-). Compound **8m** cyclized in methanolic sodium methoxide to give the corresponding 4-amino-3-chloro-5-(4-bromo-phenyl)-7-phenyl-2*H*-thiopyrano[2,3-*b*]pyridin-2-one **9m**. Other analogues **6b**,**c** reacted with **7e** to give the corresponding **8′n**,**o**, which converted to **8′n**,**om** which cyclized



m, Ar=C_6H_4-Br-4; Ar'=C_6H_5

n, Ar=C_6H_4-(NMe_2)-4; Ar'=C_6H_5

o, Ar=C_6H_4-(NMe_2)-4; Ar'=C_6H_4-CH_3-4

CHART 3

to give the corresponding **9n**,**o**, respectively. Structures **8m-o**, and **9m-o** elucidated by considering the data of IR, ^{1}H NMR and elemental analyses (cf. Experimental section and Chart 3).

The work was extended to shed more light on the chemical reactivity of the $-COOC_2H_5$ group in compounds **9c**,**g**,**k** through their reactions with hydrazine hydrate to afford the corresponding carbohydrazide derivatives **10a–c**, respectively. Chemical elucidation of the -$CONHNH_2$ group in each of **10a–c** performed through their reactions with benzaldehyde or benzylidenemalononitrile **(11)** in a separated two reactions (cf. Experimental section). The IR (cm^{-1}) of these reaction products showed no bands for -$NHNH_2$. It is important to report here that the reaction products of **10a–c** with benzaldehyde or benzylidenemalononitrile **(11)** have the same physical and chemical properties (m.p., mixed m.p.., and IR), and this confirms that the compounds **10a–c** reacted with **11** to give **13a–c** via the formation of 1:1 adduct **12a–c** followed by the loss of malononitrile. Considering the data of IR and that of elemental analyses the structure of **13a–c** was established. Moreover, the mass spectrum of **13a** as a selective example gave m/z = 527 (M^+, 11.21%) which corresponding to the molecular weight of the molecular

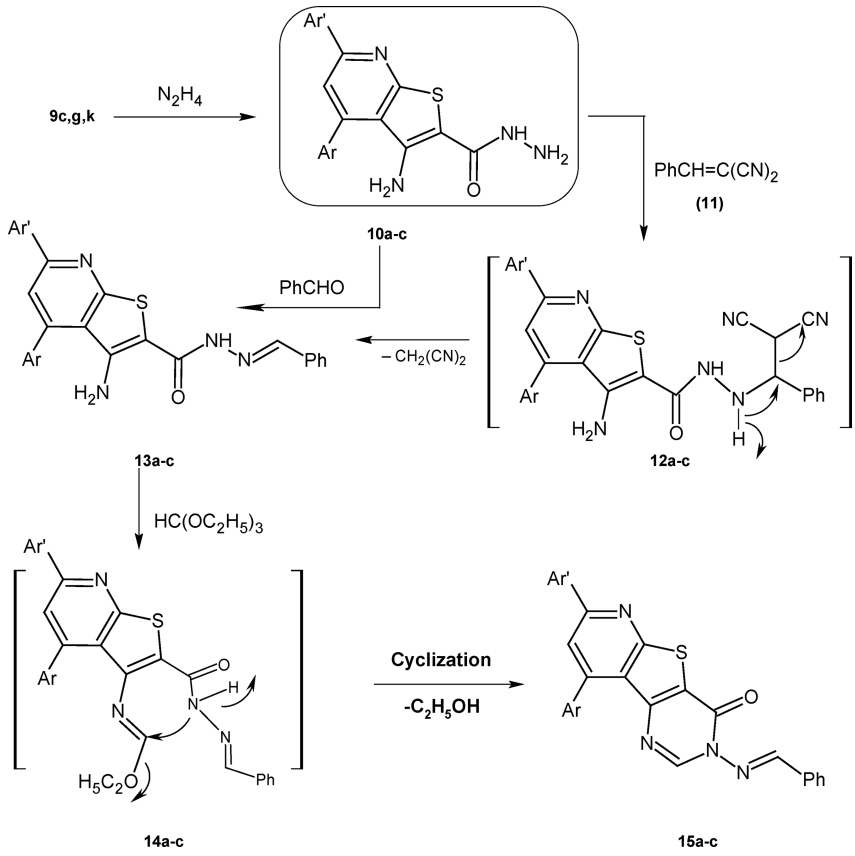


CHART 4

formula $C_{27}H_{19}BrN_4OS$ of the assigned structure, in addition to several peaks which confirm the assigned structure (cf. Chart 4 and Exp. Part).

The position and chemical reactivity of NH_2 and –NHN=CH-Ph in compounds **13a–c** confirmed through their cyclization with triethylorthoformate. The reaction seemed to be proceeded through the non-isolable products **14a–c,** which underwent cyclization through the elimination of ethanol molecule to give compounds **15a–c**. The NH and NH_2 detected in **13a–c** neither detected in IR nor ^1H NMR for compounds **15a–c**. Moreover, the mass spectrum of **15a** as a typical example gave m/z = 537 (M^+, 2.43%) which corresponding to the molecular weight of the molecular formula $C_{28}H_{17}BrN_4OS$ of the assigned structure. Considering the above mentioned data as well as that of elemental analyses

these reaction products **15a–c** formulated as pyrido[3′,2′:4,5]thieno[3,2-*d*]pyrimidinone derivatives (cf. Experimental section and Chart 4).

Further extension of this study aimed to investigate the synthetic potentiality of synthons **10a–c** via their reactions with triethyl orthoformate. Thus, it has been found **10b** reacted with triethyl orthoformate in acetic acid to afford compound **16b**. Compound **16b** is most probably formed via the reaction of **10b** with triethyl orthoformate in ratio 1 : 1 along NH_2 at thiophene 3-position to afford the non-isolable intermediate **(I)**, which cyclized spontaneously via the elimination of ethanol molecule to give the final isolated product **16b**. In a similar reaction, **10c** reacted with triethylorthoformate to afford the final isolable product **16c** whose structure was established by considering the data of IR, ^{1}H NMR, and elemental analyses (cf. Experimental section). On the other hand, **10a** reacted with triethylorthoformate under the same above-mentioned experimental conditions to afford compound **17**. The formation of compound **17** explained via the reaction of **10a** with triethylorthoformate in ratio 1 : 2 along both NH_2at thiophene 3-position and that of -$NHNH_2$to afford the non-isolable intermediate **(II)**, which cyclized spontaneously via the elimination of ethanol molecule to give the final isolated product **17**. Further confirmation of structure **17** was given through its reaction with hydrazine hydrate to afford the corresponding **16a**. Considering the data of elemental analyses, IR and ^{1}H NMR the structures of **16a–c** and **17** were elucidated (cf. Experimental section and Chart 5). Moreover, the mass spectra of **17**, **16a** and **16b** gave m/z = 505 (M^+, 26.3%), 449 (M^+, 51.11%) and 413 (M^+, 100%) respectively and these corresponding to the molecular weights of the molecular formulas $C_{24}H_{17}BrN_4O_2S$, $C_{21}H_{13}BrN_4OS$ and $C_{23}H_{19}N_5OS$ of the assigned structures, in addition to several peaks that confirm the structures of **17**, **16a,** and **16b,** respectively (cf. Chart 5 and Experimental section).

Further confirmation of the carbohydrazide group in each of **10a–c** obtained through their reactions with carbon disulfide in potassium hydroxide mixture to afford the corresponding 1,3,4-oxadiazole-2-thiol derivatives **20a–c** via the non-isolable products **18a–c** and **19a–c**. The IR of these reaction products showed no bands of CO amidic and instead the newly formed band of SH group was detected. The mass spectrum of **20c** as a typical example gave m/z = 459 (M^+, 0.65%), which corresponded to the molecular weight of the molecular formula $C_{24}H_{21}N_5OS_2$ of the assigned structure. Also, several peaks for the corresponding fragments were detected, e.g., 431, 415, 400, and 384, and this represents further elucidation of **20a–c** structures (cf. Chart 6 and Experimental section).Compounds **20a–c** reacted with hydrazine hydrate to give the corresponding **21a–c** whose structures established by

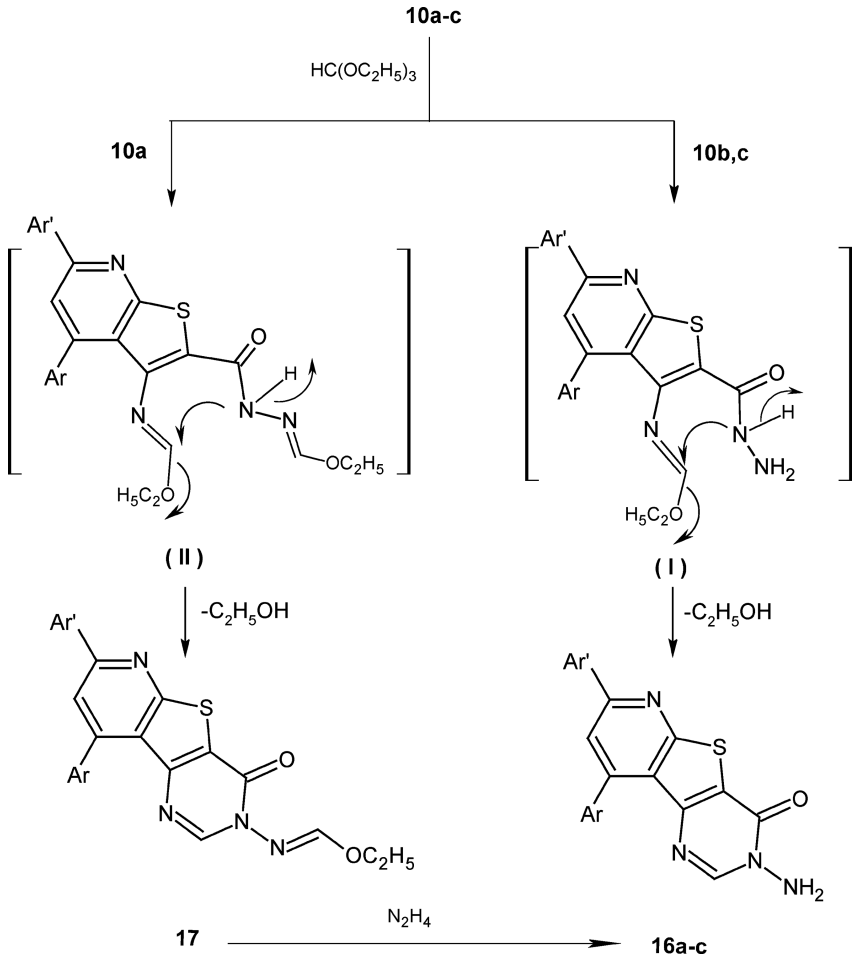


CHART 5

considering the data of IR, ^{1}H NMR and elemental analyses (cf. Experimental section). Moreover, the mass spectra of **21a**,**c** gave m/z = 495 and 457 which corresponding to the molecular weights of the molecular formulas $C_{21}H_{15}BrN_6S_2$and $C_{24}H_{23}N_7OS$ respectively of the assigned structures (cf. Chart 6 and Exp. Part).

EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded as KBr discs on Shimadzu FTIR-8201PC Spectrophotometer. ^{1}H-NMR spectra

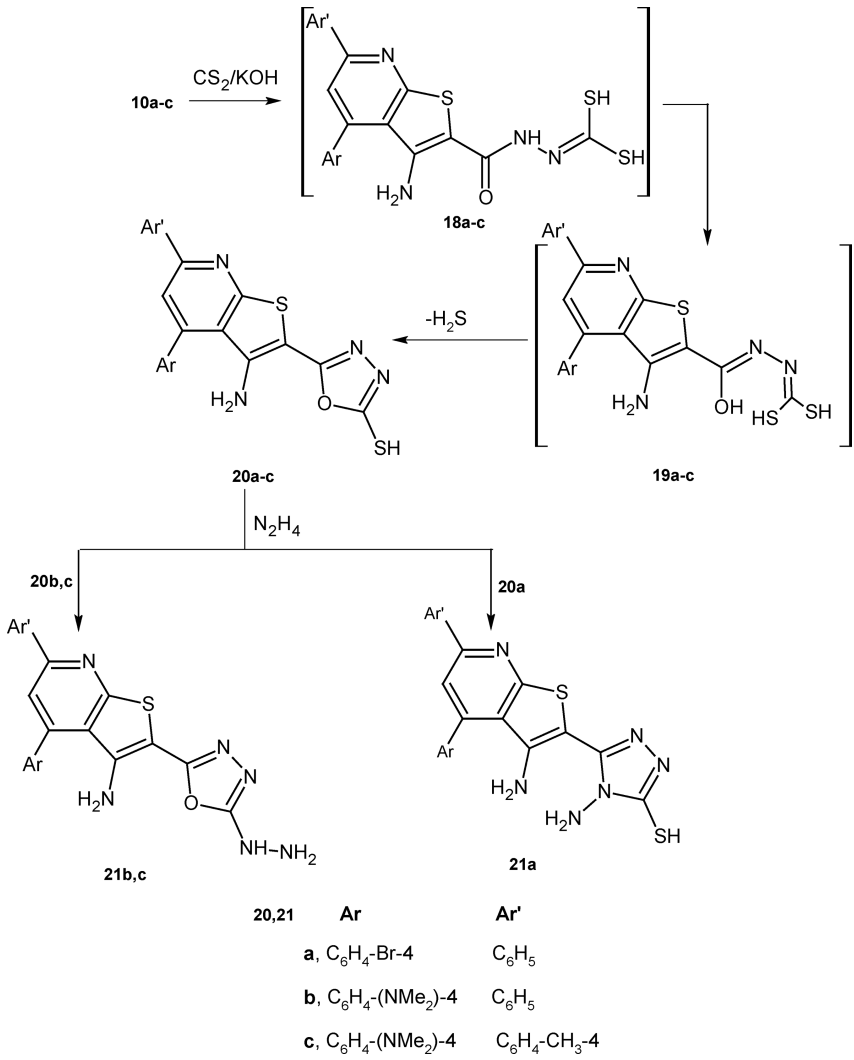


CHART 6

were recorded on Varian Mercury 300 MHz. and Varian Gemini 200 MHz. Spectrometers using TMS as an internal standard and $CDCl_3$ and DMSO-d_6 as solvents and chemical shifts are expressed as δ ppm units. Mass spectra were recorded on Shimadzu GCMS-QP1000EX using inlet type at 70 eV. The Microanalytical Center of Cairo University performed microanalyses.

Synthesis of 2-Thioxo-1,2-dihydropyridine-3-carbonitrile derivatives 6a-c—General Procedure

A solution of each of **1** (1g, 1 mmol) and **2a–c** (2.87g, 2.51g, 2.65g; 1 mmol of each respectively) in absolute ethanol (30 mL) containing a catalytic amount of piperidine (0.4 mL) was heated under reflux for 5 h. The reaction mixture was then evaporated till dryness and then cooled. The products so formed were collected by filtration, washed with cold ethanol, and then crystallized from the proper solvent to give the corresponding **6a–c**, respectively.

4-(4-Bromophenyl)-6-phenyl-2-thioxo-1,2-dihydropyridine-3-carbo-nitrile (6a)

Crystallized from acetic acid as orange crystals (69%); m.p.. 256–258°C; **IR** (ν cm^{-1}): 3151 (NH), 3059 (aromatic-CH) and 2219(CN); Anal. for $C_{18}H_{11}BrN_2S$ (367.26): Calcd./Found (%): C,58.87/58.70, H,3.02/3.0, Br,21.76/21.90, N,7.63/7.50, S,8.73/8.70.

4-[4-(Dimethylamino)phenyl]-6-phenyl-2-thioxo-1,2-dihydropyridine-3-carbonitrile (6b)

Crystallized from ethanol-dioxane as yellow crystals (69%); m.p.. 300–302°C; **IR** (ν cm^{-1}): 3291 (NH), 3059 (aromatic-CH), 2893 (sat. CH) and 2211(CN); ^{1}**H-NMR** (δppm): 2.77 (s. 6H, two CH_3), 6.45–7.56 (m, 10H, aromatic and pyridine H-5 protons) and 12.9 (s, br., 1H, NH); **MS:** 331 (M^+, 68.1%) which corresponding to the molecular weight of the molecular formula $C_{20}H_{17}N_3S$ of the assigned structure, 330 (M^+-H, 100%), 316 (M^+-CH_3, 5.8%), 301 (316-CH_3, 1.7%), 298 (M^+-SH, 1.8%) 287 (M^+-NMe_2, 7.3%), 254 (287-SH, 2.7%), 228 (M^+-PhCN, 2.8%) and 103 (PhCN, 4.6%); Anal. for $C_{20}H_{17}N_3S$ (331.43): Calcd./Found (%): C,72.48/72.20, H,5.17/5.20, N,12.68/12.70, S,9.67/9.70.

4-[4-(Dimethylamino)phenyl]-6-(4-methylphenyl)-2-thioxo-1,2-dihydro-pyridine-3-carbonitrile (6c)

Crystallized from ethanol-dioxane as reddish-orange crystals (79%); m.p.. 290–202°C; **IR** (ν cm^{-1}): 3423 (NH), 3043 (aromatic-CH) and 2211(CN); Anal. for $C_{21}H_{19}N_3S$ (345.46): Calcd./Found (%): C,73.01/73.20, H,5.54/5.40, N,12.16/12.0, S,9.28/9.30.

Synthesis of 8f, g,k,m-o—General Method

A solution of each of the reactants **A** (1.65 g, 1.72 g, 1.72 g, 1.83 g, 1.65 g, 1.73 g; 0.5 mmol of each) in sodium methoxide (prepared from 0.12 g of sodium metal in 10 mL methanol)) and reactants **B** (0.47 g,

TABLE I

Reactant A	Reactants B	Products
6b	7b	8f
6c	7b	8j
6c	7c	8k
6a	7e	8m
6b	7e	8n
6c	7e	8o

0.47 g, 0.66 g, 0.56 g, 0.56 g, 0.56 g; 0.5 mmol of each) was stirred for 2–**3** h. The products so formed were collected by filtration, washed with cold ethanol and then crystallized from the proper solvent to give the products see Table I.

2-({3-Cyano-4-[4-(dimethylamino)phenyl]-6-phenylpyridin-2-yl}thio)-acetamide (8f)

Crystallized from ethanol as pale yellow crystals (77%); m.p.. 260–262°C; **IR** (ν cm^{-1}): 3277, 3379(NH_2), 3071 (aromatic-CH), 2966 (sat. CH), 2210 (CN) and 1649 (amidic-CO); Anal. for $C_{22}H_{20}N_4OS$ (388.48): Calcd./Found (%): C,68.02/68.10, H,5.19/5.20, N,14.42/14.30, S,8.25/8.40.

2-({6-(4-methylphenyl)-3-cyano-4-[4-(dimethylamino)phenyl]pyridin-2-yl}thio)acetamide 8j

Crystallized from ethanol-dioxane as yellow crystals (72%); m.p.. 282-284°C; **IR** (ν cm^{-1}): 3202, 3382(NH_2), 3028 (aromatic-CH), 2916 (sat. CH), 2209 (CN) and 1628 (amidic-CO); Anal. for $C_{23}H_{22}N_4OS$ (402.51): Calcd./Found (%): C,68.63/68.50, H,5.51/5.30, N,13.92/14.10, S,7.97/8.10.

Ethyl ({6-(4-methylphenyl)-3-cyano-4-[4-(dimethylamino) phenyl]-pyridin-2-yl}thio)acetate 8k: Crystallized from ethanol-dioxane as pale yellow crystals (70%); m.p. 236–238°C; **IR** (ν cm^{-1}): 3071 (aromatic-CH), 2945 (sat. CH), 2210 (CN) and 1742 (ester-CO); Anal. for $C_{25}H_{25}N_3O_2S$ (431.54): Calcd./Found (%): C,69.58/69.70, H,5.84/5.90, N,9.74/9.80, S,7.43/7.40.

4-(4-Bromophenyl)-2-[(2-chloro-1-hydroxyvinyl)thio]-6-phenylnicotino-nitrile (8m)

Crystallized from ethanol as orange crystals (73%); m.p. 254–256°C; **IR** (ν cm^{-1}): 3446–3544(br. OH), 3099 (aromatic-CH) and 2220 (CN); Anal. for $C_{20}H_{12}BrClN_2OS$ (443.74): Calcd./Found (%): C,54.13/54.20, H,2.73/2.80, Br,18.01/18.10, Cl, 7.99/8.10, N,6.31/6.40, S,7.23/7.30.

TABLE II

Reactants A	Reactants B	Products
6a(1.83 g, 0.5 mmol)	7a(0.46 g, 0.5 mmol)	9a
6a(1.83 g, 0.5 mmol)	7b(0.47 g, 0.5 mmol)	9b
6a(1.83 g, 0.5 mmol)	7c(0.66 g, 0.5 mmol)	9c
6a(1.83 g, 0.5 mmol)	7d(1.16 g, 0.5 mmol)	9d
6b(1.65 g, 0.5 mmol)	7a(0.46 g, 0.5 mmol)	9e
6b(1.65 g, 0.5 mmol)	7c(066 g, 0.5 mmol)	9g
6b(1.65g g, 0.5 mmol)	7d(1.16 g, 0.5 mmol)	9h
6c(1.72 g, 0.5 mmol)	7a(0.46 g, 0.5 mmol)	9i
6c(1.72 g, 0.5 mmol)	7d(1.16 g, 0.5 mmol)	9l

2-[(2-Chloro-1-hydroxyvinyl)thio]-4-[4-(dimethylamino)phenyl]-6-phenylnicotinonitrile (8n)

Crystallized from ethanol-dioxane as orange crystals (77%); m.p. 290–292°C; **IR** (ν cm^{-1}): 3420–3540(br., OH), 3043 (aromatic-CH), 2910 (sat. CH) and 2214 (CN); ^{1}**H-NMR** (δppm): 3.08 (s, 6H, two CH_3, NMe_2), 3.71 (s, 1H, =CH-), 6.80–7.9 (m, 10H, aromatic and pyridineH-5 protons, and 13.9 (s, br. 1H, enolic OH).; Anal. for $C_{22}H_{18}ClN_3OS$ (407.91): Calcd./Found (%): C,64.78/64.90, H,4.45/4.40, Cl,8.69/8.80, N,10.30/10.40, S,7.86/7.90.

2-[(2-Chloro-1-hydroxyvinyl)thio]-4-[4-(dimethylamino)phenyl]-6-(4-methylphenyl)nicotinonitrile (8o)

Crystallized from ethanol-dioxane as orange crystals (77%); m.p. 244–246°C; **IR** (ν cm^{-1}): 3399–3465 (br., OH), 3176 (aromatic-CH), 2915 (sat. CH) and 2211 (CN); Anal. for $C_{23}H_{20}ClN_3OS$ (421.94): Calcd./Found (%): C,65.47/65.60, H,4.78/4.70, Cl,8.40/8.50, N,9.98/10.0, S,7.60/7.50.

Synthesis of 9a-e, g-i,l—General Method

A solution of each of the reactants **A** in ethanol and potassium hydroxide solution (10 mL of 10% KOH) was heated with each of reactants**B** under reflux for 2–3 h. The reaction mixture was cooled, poured into ice-cold water, acidified with hydrochloric acid. The products formed were collected by filtration, washed with water followed by cold ethanol and crystallized from the proper solvent to give the corresponding products see Table II.

Synthesis of 9f,j,k,m-o—General Procedure)

A mixture of each of **8f,j**,**k**,**m–o** (1.94 g, 2.01 g, 2.15 g, 2.21 g, 2.03 g, 2.10 g; 0.5 mmol of each) and methanolic sodium methoxide (0.11 g of sodium

with about 50 mL methanol) was heated under reflux for 5 hs. It was poured onto ice-cold water and acidified with concentrated hydrochloric acid. Collect the formed solid by filtration, wash with water and crystallize from the proper solvent to afford **9f**,**j**,**k**,**m–o**, respectively.

1-[3-Amino-4-(4-bromophenyl)-6-phenylthieno[2,3-b]pyridin-2-yl]-ethanone (9a)

Crystallized from ethanol as orange crystals, , m.p. 230–232°C; **IR** (ν cm^{-1}): 3481, 3296 (NH_2), 3050(CH-aromatic); Anal. for $C_{21}H_{15}BrN_2OS$ (423.32): Calcd./Found (%): C,59.58/60.10, H,3.57/3.70, Br,18.88/19.0, N,6.62/6.70, S,7.57/7.60.

3-Amino-4-(4-bromophenyl)-6-phenylthieno[2,3-b]pyridine-2-carbox-amide (9b)

Crystallized from ethanol as pale green crystals, m.p. 236–238°C; **IR** (ν cm^{-1}): 3482, 3312, 3166 (two NH_2), and 1668 (CO amidic); Anal. for $C_{20}H_{14}BrN_3OS$ (424.31): Calcd./Found (%): C,56.61/56.50, H,3.33/3.50, Br,18.83/18.60, N,9.90/10.0, S,7.56/7.60.

Ethyl 3-amino-4-(4-bromophenyl)-6-phenylthieno[2,3-b]pyridine-2-carboxylate 9c

Crystallized from ethanol as yellow crystals, m.p. 260-2°C; crystallize from acetic acid; **IR** (ν cm^{-1}): 3495, 3359, 3342 (NH_2), 3083(CH aromatic, 2981-2898 (CH-aliphatic) and 1666 (C=O ester); Anal. for $C_{22}H_{17}BrN_2O_2S$ (453.35): Calcd./Found (%): C,58.28/58.40, H,3.78/3.70, Br,17.63/17.80, N,6.18/6.50, S,7.07/7.10.

[3-Amino-4-(4-bromophenyl)-6-phenylthieno[2,3-b]pyridin-2-yl](4-chlorophenyl)methanone 9d

Crystallized from ethanol as orange crystals, m.p. 250–252°C; **IR** (ν cm^{-1}): 3488, 3296 (NH_2) and 3055 (CH aromatic); Anal. for $C_{26}H_{16}BrClN_2OS$ (519.84): Calcd./Found (%): C,60.07/60.10, H,3.10/3.0, Br,15.37/15.40, Cl,6.82/6.90, N,5.39/5.50, S,6.17/6.20.

1-3-Amino-4-[4-(dimethylamino)phenyl]-6-phenylthieno[2,3-b]pyridin-2-ylethanone 9e

Crystallized from ethanol as yellow crystals, m.p. 237–239°C; **IR** (ν cm^{-1}): 3459, 3303 (NH_2), and 2994–2809 (aliphatic CH); MS: 387 (M^+, 67.1%), which corresponds to the molecular weight of the molecular formula $C_{23}H_{21}N_3OS$ of the assigned structure, 386 (M^+-H, 100%), 385 (386-H, 38.0%), 371 (M^+-NH_2, 17.5%), 356 (371-CH_3, 1.8%), 343 (M^+-NMe_2, 15.5%), 344 (M^+-$COCH_3$, 9.7%), 300 (344- NMe_2, 14.4%),

284 (M^+-PhCN, 1.9%), 240 (284-NMe_2, 3.0%), 103 (PhCN, 4.0%); Anal. for $C_{23}H_{21}N_3OS$ (387.49): Calcd./Found (%): C,71.29/71.10, H,5.46/5.50, N,10.84/11.0, S,8.27/8.20.

Ethyl 3-Amino-4-[4-(dimethylamino)phenyl]-6-phenylthieno [2,3-b]-pyridine-2-carboxylate 9g

Crystallized from ethanol-dioxane as yellow crystals, m.p. 230–232°C; cIR (ν cm^{-1}): 3495, 3381 (NH_2), 2989–2889 (CH-aliphatic) and 1672 (C=O ester); ^{1}H-NMR (δppm): 1.5 (t, 3H, $\underline{CH_3}CH_2$-), 3.09 (s, 6H, NMe_2), 3.87 (q, 2H, $CH_3\underline{CH_2}$-), 5.93 (s, br., 2H, NH_2) and 6.81-8.12 (m, 10H, aromatic and pyridineH-5 protons); Anal. for $C_{24}H_{23}N_3O_2S$ (417.52): Calcd./Found (%): C,69.04/70.0, H,5.55/5.70, N,10.06/10.10, S,7.68/7.70.

[3-Amino-4-[4-(dimethylamino)phenyl]-6-phenylthieno[2,3-b]pyridin-2-yl](4-chlorophenyl)methanone 9h

Crystallized from ethanol as yellow crystals, m.p. 212–214°C; **IR** (ν cm^{-1}): 3456, 3278 (NH_2), 3061 (CH aromatic) and 2886–2807(aliphatic CH); MS: 484 (M^+, 88.8%), which corresponds to the molecular weight of the molecular formula $C_{28}H_{22}ClN_3OS$ of the assigned structure, 483 (M^+-H, 100%), 482 (483-H, 64.9%), 469 (M+-CH_3, 6.3%), 468 (483-CH_3, 6.5%), 467 (482-CH_3, 8.3%), 373 (M^+-C_6H_4-p-Cl, 1.2%), 345 (M^+-COC_6H_4-p-Cl, 1.0%), 329 (345-C_6H_4-p-Cl, 2.7%), 301 (345-NMe_2, 4.5%), 139 (COC_6H_4-p-Cl, 41.2%), 111 (C_6H_4-p-Cl, 47.3%), 103 (PhCN, 4.5%); Anal. for $C_{28}H_{22}ClN_3OS$ (484.01): Calcd./Found (%): C,69.48/70.0, H,4.58/4.60, Cl,7.32/7.40, N,8.68/8.80, S,6.62/6.70.

1-[3-Amino-4-[(4-dimethylaminophenyl)]-6-(4-methylphenyl)thieno-[2,3-b]pyridin-2-yl]ethanone 9i

Crystallized from ethanol as yellow crystals, m.p. 202–204°C; **IR** (ν cm^{-1}): 3469, 3322 (NH_2), and 2887–2807 (aliphatic CH); Anal. for $C_{24}H_{23}N_3OS$ (401.52): Calcd./Found (%): C,71.79/71.70, H,5.77/5.80, N,10.47/10.60, S,7.99/8.10.

[3-Amino-4-[4-(dimethylaminophenyl)]-6-(4-methylphenyl)thieno[2,3-b]pyridin-2-yl](4-chlorophenyl)methanone (9l)

Crystallized from ethanol as yellow crystals, m.p. 234–236°C; **IR** (ν cm^{-1}): 3466, 3295 (NH_2), 3027 (CH aromatic), and 2911–2805 (aliphatic CH); Anal. for $C_{29}H_{24}ClN_3OS$ (498.03): Calcd./Found (%): C,69.94/70.10, H,4.86/4.90, Cl,7.12/7.30, N,8.44/8.60, S,6.44/6.60.

3-Amino-4-[4-(dimethylamino)phenyl]-6-phenylthieno[2,3-b]pyridine-2-carboxamide (9f)

Crystallized from ethanol as yellow crystals, m.p. 260°C; **IR** (ν cm^{-1}): 3466, 3428, 3358 (two NH_2), 2966–2806 (aliphatic CH) and 1654 (CO amide); Anal. for $C_{22}H_{20}N_4OS$ (388.48): Calcd./Found (%): C,68.02/68.10, H,5.19/5.20, N,14.42/14.40, S,8.25/8.40.

3-Amino-4-[4-(dimethylamino)phenyl]-6-(4-methylphenyl)thieno[2,3-b]pyridine-2-carboxamide 9j

Crystallized from ethanol-dioxane as orange crystals, m.p. 280°C; **IR** (ν cm^{-1}): 3454, 3379, 3330 (two NH_2), 2965–2800 (aliphatic CH) and 1650 (CO amide); Anal. for $C_{23}H_{22}N_4OS$ (402.51): Calcd./Found (%): C,68.63/68.70, H,5.51/5.60, N,13.92/14.10, S,7.97/8.10.

Ethyl 3-Amino-4-(dimethylaminophenyl)-6-(4-methylphenyl)thieno-[2,3-b]pyridine-2-carboxylate (9k)

Crystallized from ethanol-dioxane as yellow crystals, m.p. 268°C; **IR** (ν cm^{-1}): 3481, 3357 (NH_2), 3026 (aromatic CH0, 2976–2803 (CH-aliphatic) and 1681 (C=O ester); Anal. for $C_{25}H_{25}N_3O_2S$ (431.54): Calcd./Found (%): C,69.58/69.60, H,5.84/5.70, N,9.74/9.80, S,7.43/7.50.

4-Amino-5-(4-bromophenyl)-3-chloro-7-phenyl-2H-thiopyrano[2,3-b]-pyridin-2-one (9m)

Crystallized from ethanol-dioxane as yellow crystals, m.p. > 300°C; **IR** (ν cm^{-1}): 3484, 3383 (NH_2), and 1671 (CO); Anal. for $C_{20}H_{12}BrClN_2OS$ (443.74): Calcd./Found (%): C,54.13/54.20, H,2.73/2.80, Br,18.01/18.10, Cl,7.99/8.10, N,6.31/6.40, S,7.23/7.40.

4-Amino-3-chloro-5-[4-(dimethylamino)phenyl]-7-phenyl-2H-thiopyrano-[2,3-b]pyridin-2-one (9n)

Crystallized from ethanol as yellow crystals, m.p. 230°C; **IR** (ν cm^{-1}): 3485, 3363 (NH_2), 3039 (aromatic CH), 2977–2807 (aliphatic CH), and 1666 (CO); ^{1}**H NMR** (δppm): 3.06 (s, 6H, two CH_3, NMe_2), 5.92 (s, br., 2H, NH_2) and 6.81-8.12 (m, 10H, aromatic and pyridineH-5 protons); Anal. for $C_{22}H_{18}ClN_3OS$ (407.91): Calcd./Found (%): C,64.78/64.80, H,4.45/4.50, Cl,8.69/8.70, N,10.30/10.40, S,7.86/7.90.

4-Amino-3-chloro-5-[4-(dimethylamino)phenyl]-7-(4-methylphenyl)-2H-thiopyrano[2,3-b]pyridin-2-one (9o)

Crystallized from ethanol as yellow crystals, m.p. 272°C; **IR** (ν cm^{-1}): 3485, 3363 (NH_2), 3029 (aromatic CH), 2982–2805 (aliphatic CH),

and 1666 (CO); Anal. for $C_{23}H_{20}ClN_3OS$ (421.94): Calcd./Found (%): C,65.47/65.50, H,4.78/4.80, Cl,8.40/8.50, N,9.96/10.10, S,7.60/7.60.

Synthesis of Thieno[2,3-*b*]pyridine-2-carbohydrazide Derivatives 10a-c—General Procedure

compounds **9c, g g,k** (1.13 g, 1.04 g, 1.07 g; 0.25 mmol of each) and hydrazine hydrate 95% (5 mL) were heated under reflux for 5h. The reaction mixture evaporated to half of its volume and allowed to cool. The solid products formed collected by filtration and recrystallized from the proper solvent.

3-Amino-4-(4-bromophenyl)-6-phenylthieno[2,3-b]pyridine-2-carbo-hydrazide (10a)

Crystallized from ethanol as yellow crystals (62%); m.p. 242–244°C; **IR** (ν cm^{-1}): 3484, 3460, 3424, 3328 (NH_2 and NH), and 3037 (CH aromatic); Anal. for $C_{20}H_{15}BrN_4OS$ (439.3): Calcd./Found (%): C,54.68/54.50, H,3.44/3.50, Br,18.19/18.30, N,12.75/12.60, S,7.30/7.40.

3-Amino-4-[4-(dimethylamino)phenyl]-6-phenylthieno[2,3-b]pyridine-2-carbohydrazide (10b)

Crystallized from ethanol as orange crystals (69%); m.p. 220°C; **IR** (ν cm^{-1}): 3475, 3397, 3346, 3348 ($NH_2$and NH), and 3038 (CH aromatic); ^{1}**H-NMR** (δppm): 2.97 (s, 6H, NMe_2), 3.14 (s, br., 3H, NH-NH_2), 6.05 (s, br. 2H, NH_2 at position-3), 6.81–8.10 (m, 10H, aromatic and pyridineH-5 protons); Anal. for $C_{22}H_{21}N_5OS$ (403.5): Calcd./Found (%): C,65.49/65.50, H,5.25/5.10, N,17.36/17.50, S,7.95/8.0.

3-Amino-4-[4-(dimethylamino)phenyl]-6-(4-methylphenyl)thieno[2,3-b]pyridine-2-carbohydrazide (10c)

Crystallized from ethanol as orange crystals (59%); m.p. 220°C; **IR** (ν cm^{-1}): 3471, 3316, ($NH_2$and NH), and 3037 (CH aromatic); Anal. for $C_{23}H_{23}N_5OS$ (417.5): Calcd./Found (%): C,66.16/66.2, H,5.55/5.6, N,16.77/16.5, S,7.68/7.8.

Synthesis of *N′*-(phenylmethylene)thieno[2,3-*b*]pyridine-2-carbohydr-azide derivatives 13a-c—General Procedure)

A solution of each **10a–c** (2.19 g, 2.01 g, 2.08 g; 0.5 mmol of each) in acetic acid (50 mL) with benzaldehyde (0.54 g) or benzyldenemalononitrile **11** (0.77 g); 0.5 mmol of each. The reaction mixture heated under reflux

for 3 hrs. The solid products so formed were collected by filtration and crystallized from proper solvent to afford **13a-c,** respectively.

3-Amino-4-(4-bromophenyl)-6-phenyl-N′-(phenylmethylene)thieno-[2,3-b]pyridine-2-carbohydrazide (13a)

Crystallized from DMF-ethanol mixture as orange crystals (54%); m.p. 300°C; **IR** (ν cm^{-1}): 3479, 3325 (NH_2, and NH), and 1624 (CO hydrazidic); **MS**: 527 (M^+, 11.21%) which corresponding to the molecular weight of the molecular formula $C_{27}H_{19}BrN_4OS$ of the assigned structure, 528 (M+1, 34.96%), 529 (M+2, 10.23%), 408 (M^+-Ph-CH=N-NH, 94.11%), 407 (408-H, 27.95%), 406 (407-H, 100%), and 379 (407-CO, 39.99%), 119 (Ph-CH=N-NH, 22.59%), 103 (PhCN, 13.88%); Anal. for $C_{27}H_{19}BrN_4OS$ (527.4): Calcd./Found(%): C,61.48/61.50, H,3.63/3.60, N,10.62/10.50 S,10.62/10.50, Br,15.15/15.20.

3-Amino-4-[4-(dimethylamino)phenyl-6-phenyl-N′-(phenylmethylene)-thieno[2,3-b]pyridine-2-carbohydrazide (13b)

Crystallized from dioxane-ethanol as orange crystals (59%); m.p. 290–292°C; **IR** (ν cm^{-1}): 3468, 3315, 3150 (NH_2 and NH), and 3041 (CH aromatic); Anal. for $C_{29}H_{25}N_5OS$ (491.6): Calcd./Found (%): C,70.85/71.0, H,5.13/5.20, N,14.29/14.40, S,6.52/6.60.

3-Amino-4-[4-(dimethylamino)phenyl-6-(4-methylphenyl)-N′-(phenylmethylene)thieno[2,3-b]pyridine-2-carbohydrazide (13c)

Crystallized from dioxane as yellow crystals (59%); m.p. 290–292°C; **IR** (ν cm^{-1}): 3468, 3308, 3149 ($NH_2$and NH), and 3029 (CH aromatic); Anal. for $C_{30}H_{27}N_5OS$ (505.6): Calcd./Found (%): C,71.26/71.10, H,5.38/5.40, N,13.85/13.90, S,6.34/6.40.

Synthesis of 15a–c 16b,c, and 17—General Procedure

A solution of each of **13a-c** (1.31 g, 1.25 g, 1.26 g), **10b,c** (1.01 g, 1.04 g), and**10a** (1.09 g); 0.25 mmol of each; in glacial acetic acid (30–50 mL) and triethyl orthoformate (1.48 g, 1 mmol) was heated under reflux 5 hs. The reaction mixture evaporated to its half volume then cooled with ice-cold water. The solid product isolated in each case collected by filtration, washed with ethanol and crystallized from the proper solvent to yield **15a-c, 16b,c,** and **17,** respectively.

Synthesis of 16a

A mixture of **17** (1.26g, 0.25 mmol) and hydrazine hydrate (15-20 mL) was heated under reflux for 5-7 hs. The product so formed after cooling was filtered off, washed with cold ethanol, and crystallized from the acetic acid to give **16a**.

9-(4-Bromophenyl)-7-phenyl-3-[(phenylmethylene)amino]pyrido[3′,2′-:4,5]thieno[3,2-d]pyrimidin-4(3H)-one (15a)

Crystallized from acetic acid as colorless crystals (59%); m.p. 320°C; **IR** (ν cm^{-1}): 3061 (CH aromatic) and 1667 (CO); ^{1}**H-NMR** (δppm): 7.27–7.87 (m, 15H, aromatic and pyridineH-5 protons), 8.31 (s, 1H, Pyrimidine-CH) and 9.72 (s, 1H, -CH=N); **MS**: 537 (M^+, 2.43%) which corresponding to the molecular weight of the molecular formula $C_{28}H_{17}BrN_4OS$ of the assigned structure, 538 (M+1, 5%), 539 (M+2, 1.99%), 433 (M^+-Ph-CH=N, 95.34%), 435 (539-Ph-CH=N, 51.09%), and 378 (433-CHNCO, 11.51%); 104 (Ph-CH=N, 25.69%), 103 (PhCN, 83.20%), 77 (Ph, 100%), Anal. for $C_{28}H_{17}BrN_4OS$ (537.4): Calcd./Found (%): C,62.58/62.60, H,3.19/3.20, Br,14.87/15.0, N,10.42/10.40, S,5.97/6.10.

9-(4-Dimethylaminophenyl)-7-phenyl-3-[(phenylmethylene)amino]-pyrido[3′,2′:4,5]thieno[3,2-d]pyrimidin-4(3H)-one (15b)

Crystallized from dioxane as yellow crystals (59%); m.p. 310–312°C; **IR** (ν cm^{-1}): 3052 (CH aromatic) and 1671 (CO); Anal. for $C_{30}H_{23}N_5OS$ (501.6): Calcd./Found (%): C,71.83/72.0, H,4.62/4.70, N,13.96/14.0, S,6.39/6.40.

9-(4-Dimethylaminophenyl)-7-(4-methylphenyl)-3-[(phenylmethylene)-amino]pyrido[3′,2′:4,5]thieno[3,2-d]pyrimidin-4(3H)-one (15c)

Crystallized from dioxane as orange crystals (59%); m.p. 307–309°C; **IR** (ν cm^{-1}): 3023 (CH aromatic), 2916–2855 (aliphatic CH) and 1663 (CO); Anal. for $C_{31}H_{25}N_5OS$ (515.6): Calcd./Found (%): C,72.21/72.20, H,4.89/4.80, N,13.58/13.60, S,6.22/6.20.

Ethyl [9-(4-Bromophenyl)-4-oxo-7-phenylpyrido[3′,2′:4,5]thieno[3,2-d]pyrimidin-3(4H)-yl]imidoformate 17

Crystallized from acetic acid as yellowish-white crystals (55%); m.p. > 300°C; **IR** (ν cm^{-1}): 3060 (CH aromatic), 2990 (aliphatic CH)

and 1668 (CO); **^{1}H-NMR** (δppm): 1.44 (t, 3H, $COOCH_2\underline{CH_3}$, J = 7.2), 4.43 (q, 2H, $COO\underline{CH_2}CH_3$, J =7 .2), 7.26–8.17 (m, 10H, aromatic and pyridineH-5 protons), 8.18 (s, 1H, Pyrimidine-CH) and 8.73 (s, 1H, -CH=N); **MS**: 505 (M^+, 26.3%) which corresponds to the molecular weight of the molecular formula of the assigned structure, 506 (M+1,23.7%), 507 (M+2, 25.7%), 460 (M^+-OC_2H_5, 6.8%), 461 (506-OC_2H_5, 7.0%), 462 (507-OC_2H_5, 4.4%), 447 (505-$CHOC_2H_5$, 0.9%), 448 (506-$CHOC_2H_5$, 1.1%), (433 (M^+-N=CH-OC_2H_5, 100%), 434 (506-N=CH-OC_2H_5, 94.3%), 435 (507-N=CH-OC_2H_5, 34.2%), 380 (435- CON-CH=, 5.0%), 379 (434- CON-CH=, 11.7%), 378 (433-CON-CH=, 12.3%), 103 (PhCN, 3.7%), 72 (-N=CH-OC_2H_5, 7.4%); Anal. for $C_{24}H_{17}BrN_4O_2S$ (505.38): Calcd./Found (%): C,57.04/57.12, H,3.39/3.40, Br,15.81/15.90, N,11.09/11.10, S,6.34/6.40.

3-Amino-9-(4-bromophenyl)-7-phenylpyrido[3′,2′:4,5]thieno[3,2-d]-pyrimidin-4(3H)-one 16a

Crystallized from dioxane as pale yellow crystals (50%); m.p. >300°C; **IR** (ν cm^{-1}): 3315, 3261, 3208 (NH_2), 3039 (CH aromatic), 2852 (aliphatic CH), and 1668 (CO); **^{1}H-NMR** (δppm): 6.08 (s, br., 2H, NH_2), 7.53-8.28 (m, 10H, aromatic and pyridineH-5 protons) and 8.39 (s, 1H, Pyrimidine-CH); **MS**: 449 (M^+, 51.11%), which corresponds to the molecular weight of the molecular formula $C_{21}H_{13}BrN_4OS$ of the assigned structure, 450 (M+1, 100%), 451 (M+2, 24.01%), 448 (M^+-H, 93.40%), 419 (448-NNH, 33.63%), 85 [-N=CH-N(NH_2)CO, 29.41%], 72 (COCS, 38.31%), 57 (-N-CH=N-NH_2, 60.43%); Anal. for $C_{21}H_{13}BrN_4OS$ (449.32): Calcd./Found (%): C,56.13/56.20, H,2.92/3.0, Br,17.78/17.90, N,12.47/12.50, S,7.14/7.20.

3-Amino-9-[4-(dimethylamino)phenyl]-7-phenylpyrido[3′,2′:4,5]thieno-[3,2-d]pyrimidin-4(3H)-one 16b

Crystallized from alcohol-dioxane as yellow crystals (58%); m.p. 310°C; **IR** (ν cm^{-1}): 3326, 3278, 3212 (NH_2), 3054 (CH aromatic), 2890 (aliphatic CH), and 1674 (CO); **^{1}H-NMR** (δppm): 3.07 (s, 6H, -NMe_2), 6.11(s, br., 2H, NH_2), 6.84–8.05 (m, 10H, aromatic and pyridineH-5 protons) and 8.44 (s, 1H, Pyrimidine-CH); **MS**: 413 (M+, 100%), which corresponds to the molecular weight of the molecular formula $C_{23}H_{19}N_5OS$ of the assigned structure, 412 (M^+-H, 20.50%), 397 (M^+-NH_2, 6.45%), 370 (M^+-NH_2-N-CH=, 27.11%), and 328 (370-CON-, 11.29%); Anal. for $C_{23}H_{19}N_5OS$ (413.49): Calcd./Found (%): C,66.81/66.90, H,4.63/4.70, N,16.94/17.0, S,7.75/7.80.

3-Amino-9-[4-(dimethylamino)phenyl]-7-(4-methylphenyl)pyrido-[3′,2′:4,5]thieno[3,2-d]pyrimidin-4(3H)-one 16c

Crystallized from dioxane as yellow crystals (52%); m.p. 280°C; **IR** (ν cm^{-1}): 3447, 3314, 3202 (NH_2), 3032 (CH aromatic), 2917 (aliphatic CH), and 1667 (CO); Anal. for $C_{24}H_{21}N_5OS$ (427.52): Calcd./Found (%): C,67.43/67.50, H,4.95/5.0, N,16.38/16.40 S,7.50/7.6.

Synthesis of 1,3,4-Oxadiazol-2-thiols 20a-c—General Procedure

Carbon disulfide (0.76 g, 1 mmol) was added to a solution of potassium hydroxide (0.56 g, 1 mmol), absolute ethanol (50 mL) and each 10a-c (2.19 g, 2.01 g, 2.08 g; 0.5 mmol). Dilute this mixture with about 50 mL absolute ethanol, stir at room temperature for 5-7 hs. Leave overnight, collect the products formed by filtration, wash with ethanol, and crystallize with the proper solvent.

5-[3-Amino-4-(4-bromophenyl)-6-phenylthieno[2,3-b]pyridin-2-yl]-1,3,4-oxadiazole-2-thiol 20a

Crystallized from dioxane as orange crystals (53%); m.p. 280°C; IR (ν cm^{-1}): 3250–3550 (broad band NH_2, SH), 1653 (C=N) and 1613 (C=C); MS: 422 (M^+-HS-C=N, 10%), 406 (422-O, 86.9%), 404 [M^+-O(HS)C=N-N=, 86.1%], 380 (M+-oxadiazolyl-2-thiol, 8.6%), 103 (PhCN, 12.5%) and 73 (=N-N=C-SH, 17%); Anal. for $C_{21}H_{13}BrN_4OS_2$ (481.38): Calcd./Found (%): C,52.40/52.50, H,2.72/2.80, Br,16.60/16.50, N,11.64/11.40, S,13.32/13.40.

5-{3-Amino-4-[4-(dimethylamino)phenyl]-6-phenylthieno[2,3-b]pyrid-in-2-yl}-1,3,4-oxadiazole-2-thiol 20b

Crystallized from dioxane as orange crystals (51%); m.p. 280°C; **IR** (ν cm^{-1}): 3150–3471 (broad band NH_2, SH) and 1607 (C=C); Anal. for $C_{23}H_{19}N_5OS_2$ (445.55): Calcd./Found (%): C,62.00/62.10, H,4.30/4.20, N,15.72/15.80 S,14.39/14.40.

5-{3-Amino-4-[4-(dimethylamino)phenyl]-6-(4-methylphenyl)thieno-[2,3-b]pyridin-2-yl}-1,3,4-oxadiazole-2-thiol 20c

Crystallized from dioxane as brown crystals (62%); m.p. 260°C; **IR** (ν cm^{-1}): 3179–3464 (broad band NH_2, SH) and 1608 (C=C); **MS**: 459 (M^+, 0.65%), which corresponds to the molecular weight of the molecular formula $C_{24}H_{21}N_5OS_2$of the assigned structure, 457 (M^+-2H, 0.56%), 431 (M-N_2, 1.02%), 415 (M^+- NMe_2, 1.69%), 400 (415-CH_3, 5.43%), 384

(457-N_2, =CSH, 100%), 368 (384-O, 6.67%), 324 (368-NMe_2, 1.86%); Anal. for $C_{24}H_{21}N_5OS_2$ (459.58): Calcd./Found (%): C,62.72/62.80, H,4.61/4.50, N,15.24/15.30 S,13.95/14.00.

Synthesis of 21a–c

A mixture of each of 20a-c (1.20 g, 1.11 g, 1.15 g; 0.25 mmol of each) and hydrazine hydrate (15–20 mL) was heated under reflux for 5–7 hs. The products so formed after cooling were filtered off, washed with cold ethanol, and crystallized from the proper solvent to give 21a–c.

4-Amino-5-[3-amino-4-(4-bromophenyl)-6-phenylthieno[2,3-b]pyrid-in-2-yl]-4H-1,2,4-triazole-3-thiol 21a

Crystallized from dioxane as orange crystals (57%); m.p. 324°C; **IR** (ν cm^{-1}): 2761–3452 (broad band NH_2, SH) and 1604 (C=C); **MS**: 494 (M^+-1, 18.84%), which corresponds to the loosing of H from the parent peak, 462 (M^+-SH, 4.91%), 405 (M^+-HNCS, N-NH_2, 7.55%), 380 (M^+- triazole ring, 11.32%), 59 (HNCS, 34.34%), 60 (HS-N=CH_2, 100%); Anal. for $C_{21}H_{15}BrN_6S_2$ (495.41): Calcd./Found (%): C,50.91/51.0, H,3.05/3.10, Br,16.13/16.20, N,16.96/17.10, S,12.94/13.0.

4-(4-Dimethylaminophenyl)-2-(5-hydrazino-1,3,4-oxadiazol-2-yl)-6-phenylthieno[2,3-b]pyridin-3-amine 21b

Crystallized from ethanol as orange crystals (52%); m.p. 200°C; **IR** (ν cm^{-1}): 3387, 3261 (NH_2, NH) and 1608 (C=C); Anal. for $C_{23}H_{21}N_7OS$ (443.52): Calcd./Found (%): C,62.28/62.40, H,4.77/4.50, N,22.11/22.10, S,7.23/7.40.

4-(4-Dimethylaminophenyl)-2-(5-hydrazino-1,3,4-oxadiazol-2-yl)-6-(4-methylphenyl)thieno[2,3-b]pyridin-3-amine 21c

Crystallized from ethanol as orange crystals (58%); m.p. 210°C; **IR** (ν cm^{-1}): 3466, 3300 (NH_2, NH), and 1610 (C=C); ^{1}**H NMR** (δppm): 0.95 (s, 3H, CH_3), 2.84 (s, 6H, NMe_2), 4.90 (s, br., 2H, NH_2 at thiophene), 5.44 (s, br., 2H, $\underline{NH_2}NH$), 5.73 (s, br., 1H, $\underline{NH}NH_2$), and 6.51–7.70 (m, 9h, aromatic and Pyridine H-5); **MS:** 457 (M^+, 1.88%), which corresponds to the molecular weight of the molecular weight $C_{24}H_{23}N_7OS$ of the assigned structure, 441 (M^+-NH_2), 426 (M^+-NH_2NH, 8.85%), 429 (M^+-N_2, 5.50%), 413 (M^+-NMe_2), 359 (M^+-oxadiazole residue, 100%), 315 (359-NMe_2, 36%); 314 (359-oxadiazole, CS, 34%), 143 (M+-314, 2.73%); Anal. for $C_{24}H_{23}N_7OS$ (457.55): Calcd./Found (%): C,63.00/63.10, H,5.07/5.10, N,21.43/21.30, S,7.01/7.10.

REFERENCES

[1] A. Adreani, A. Leani, and G. Ville, *Eur. J. Med. Chem.*, **35,** 77 (2000).
[2] E. A. Bekhite and A. M. Baraka, *Eur. J. Med. Chem.*, **40,** 1405 (2005).
[3] A. Krauze, R. Vitolina, V. Garaliene, L. Stile, V. Klusa, and G. Duburs, *Eur. J. Med. Chem.*, **40,** 1163 (2005).
[4] A. E. Abdel-Rahman, E. A. Bekhite, and E. A. Al-Tafi, *Pharmazie*, **58,** 372 (2003).
[5] G. P. Moloney, *Molecules*, **6,** 203 (2001).
[6] J. M. Quintela, C. Prinador, C. Veiga, L. Gonzales, L. M. Botana, A. Alfonso, and R. Riguera, *Bioorg. Med. Chem.*, **6,** 1911 (1998).
[7] J. M. Quintela, C. Prinador, L. Gonzales, A. Parama, F. Alvares, M. L. Sammartin, and R. Riguera, *Eur. J. Med. Chem.*, **38,** 265 (2003).
[8] F. A. Attaby, *Arch. Pharmcol. Res.*, **13,** 342 (1990).
[9] F. A. Attaby, L. I. Ibrahim, S. M. Eldin, and A. K. K El-Louh, *Phosphorous, Sulfur and Silicon*, **73,** 127 (1992).
[10] F. A. Attaby, S. M. Eldin, and M. Abdel Razik; *Phosphorous, Sulfur, and Silicon*, **106,** 21 (1994).
[11] F. A. Attaby and A. M. Abdel-Fattah, *Phosphorous, Sulfur, and Silicon*, **119,** 257 (1996).
[12] F. A. Attaby; *Phosphorous, Sulfur, and Silicon*, **126,** 27 (1997).
[13] F. A. Attaby; *Phosphorous, Sulfur, and Silicon*, **139,** 1 (1998).
[14] F. A. Attaby, S. M. Edin, and M. A. A. Elneairy, *Heteroatom Chemistry*, **9,** 571 (1998).
[15] F. A. Attaby, S. M. Edin, and M. A. A. Elneairy, *J. Chem. Res. (M)*, **10,** 2754; *J. Chem. Res. (S)*, **10** (1998).
[16] F. A. Attaby, M. A. A. Elneairy, and M. S. Elsayed, *Phosphorous, Sulfur, and Silicon*, **149,** 230 (1999).
[17] F. A. Attaby and A. M. Abdel-Fattah, *Phosphorous, Sulfur, and Silicon*, **155,** 253 (1999).
[18] M. A. A. Elneairy, S. M. Eldin, F. A. Attaby, and A. K. K. El-Louh, *Phosphorous, Sulfur, and Silicon*, **167,** 289 (2000).
[19] M. A. A. Elneairy, F. A. Attaby, and M. S. Elsayed, *Phosphorus, Sulfur, and Silicon*, **167,** 161 (2000).
[20] F. A. Attaby, M. A. A. Elneairy, S. M. Eldin, and A. K. K. El-Louh, *J. C. C. S. (China)*, **48**(5), 893 (2001).
[21] F. A. Attaby, H. M. Mostafa, A. H. H. Elghandour, and Y. M. Ibrahem, *Phosphorus, Sulfur, and Silicon*, **177,** 2753 (2002).
[22] F. A. Attaby, A. H. H. Elghandour, H. M. Mustafa, and Y. M. Ibrahem, *J. C. C. S. (China)*, **49**(4), 561 (2002).
[23] F. A. Attaby, S. M. Eldin, M. A. A. Elneairy, and A. K. K. Elouh, *Phosphorus, Sulfur, and Silicon*, **179,** 2205 (2004).
[24] F. A. Attaby, A. H. H. Elghandour, M. A. Ali, and Y. M. Ibrahem, *Phosphorus, Sulfur, and Silicon*, **181,** 1 (2006).
[25] F. A. Attaby, Ali M. A., A. H. H. Elghandour, and Y. M. Ibrahem, *Phosphorus, Sulfur, and Silicon*, **181,** 1087 (2006).
[26] F. A. Attaby, A. H. Elghandour, M. A. Ali, and Y. M. Ibrahem, *Phosphorus, Sulfur, and Silicon*, **182,** 133 (2007).
[27] F. A. Attaby, A. H. H. Elghandour, M. A. Ali, and Y. M. Ibrahem; *Phosphorus, Sulfur, and Silicon*, **182,** 695 (2007).
[28] F. A. Attaby, M. M. Ramla, and E. M. Gouda, *Phosphorus, Sulfur, and Silicon*, **182,** 517 (2007).

[29] M. A. Gad-Elkareem, A. M. Abdel-Fattah, and M. A. A. Elneairy, *Phosphorus, Sulfur, and Silicon*, **181,** 891 (2006).
[30] M. A. A. Elneairy, M. A. Gad-Elkareem, and A. M. Abdel-Fattah, *Phosphorus, Sulfur, and Silicon*, **181,** 1451 (2006).
[31] A. M. Abdel-Fattah, M. A. A. Elneairy, and M. A. Gad-Elkareem, *Phosphorus, Sulfur, and Silicon*; **182,** 1351 (2007).
[32] A. M. Shestopalov, V. K. Pronomenkov, Yu. A. Sharanin, L. A. Rodinovskaya, and S. Yu. Sharanin, *Zh. Org. Khim.* **20,** 1517 (1984);*Chem. Abstr.*, **102,** 62,106x (1985).
[33] A. M. Shestopalov and Yu. A. Sharanin, *Zh. Org. Khim.* **20,** 1991 (1984); *Chem. Abstr.*, **102,** 95563x (1985).
[34] V. K. Pronomenkov, A. M. Shestopalov, Yu. A. Sharanin, V. P. Litvinov, L. A. Rodinovskaya, B. M. Zolotarev, V. D. Sokovykh, B. V. Rozynov, and Ya. Ya. Krymskii, *Zh. Org. Khim.* **20,** 1517 (1984); *Chem. Abstr.*, **105**, 97282r (1986).
[35] A. M. Shestopalov, Yu. A. Sharanin, and V. K. Pronomenkov, *Khim. Geterotsikl. Soedin.*, **3,** 370 (1990); *Chem. Abstr.*, **113,** 115, 034h (1990).