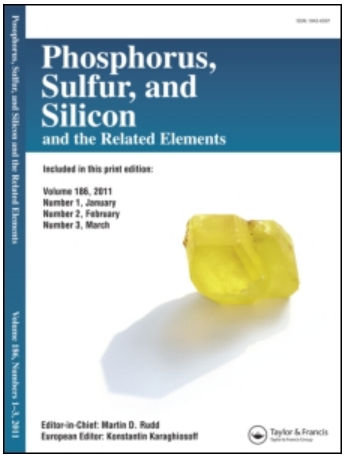

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Cyanothioacetamide in Heterocyclic Chemistry: Synthesis of Thiopyran, Pyridinethione, Thienopyridine, Pyridothienotriazine and Pyridothienopyrimidine Derivatives

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CYANOTHIOACETAMIDE IN HETEROCYCLIC CHEMISTRY: SYNTHESIS OF THIOPYRAN, PYRIDINETHIONE, THIENOPYRIDINE, PYRIDOTHIENOTRIAZINE AND PYRIDOTHIENOPYRIMIDINE DERIVATIVES

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Cyanothioacetamide (**1**) reacted with α- and β-naphthaldehyde **2a,b** to afford the corresponding 3-naphthyl-2-thiocarboxamidopropenonitriles **3a,b**. Compounds **3a,b** structures could be elucidated via their reactions with acrylonitrile, ethyl acrylate (**4a,b**), N-arylmaleimides **6a-c** and ethyl acetoacetate (**8**). The isolated products could be represented as the thiopyran, thiopyranopyrrolidine and pyridinethione derivatives **5a-d**, **7a-f** and **9a,b** respectively. Pyridinethiones **9a,b** had been used as the starting materials in the present study in addition to the next ones to synthesize several new thienopyridines, pyridothienotriazine and pyridothienopyrimidines **12a-f**, **15a,b**, **16b**, **17–19a,b** respectively through their reactions with the corresponding reagents.

All structures of the newly synthesized heterocyclic compounds were established on the basis of the data of IR, ^{1}H NMR and elemental analyses.

Keywords: Propenonitriles; Thiopyrans; Thiopyranopyrrolidines; Pyridinethiones; Thienopyridines; Pyridothienotriazines and pyridothienopyrimidines

INTRODUCTION

Several publications had appeared concerning the synthesis of pyridinethiones through the reaction of cyanothioacetamide, aldehydes and

* To receive any correspondence.

dicarbonyl derivatives, but no approach using α- and β- naphthaldehyde was reported. In continuation to our previous work[1-9] we wish to report here a new and convenient method for the preparation of pyridinethiones **9a,b** via the reaction of 3-naphthyl-2-thiocarboxamidopropenonitriles **3a,b** and ethyl acetoacetate (**8**). The reported biological activities of triazines as antiepileptic drugs[10], as herbicides[11], antioxidants[12]; neurotoxicity and antifungal activities,[13,14] of pyridinethiones as well as the reported biological activities of thienopyridines[15-17] stimulated our interest to synthesize several derivatives of these ring systems.

RESULTS AND DISCUSSION

It has been found that cyanothioacetamide (**1**) reacted with α-naphthaldehyde (**2a**) in absolute ethanol containing the catalytic amount of piperidine at room temperature to afford the corresponding 3-(α-naphthyl)-2-thiocarboxamidopropenonitrile **3a** in a good and very pure yield. The IR spectrum of **3a** showed the bands of NH_2 and CN groups and its ^1H NMR spectrum revealed the signals of NH_2, vinylic and aromatic protons. Moreover, its mass spectrum gave m/z=238 that agreed with the molecular weight of a molecular formula $C_{14}H_{10}N_2S$ of the assigned structure (cf. Table II and Chart 1). Under similar experimental condition the synthon 3-(β-naphthyl)-2-thiocarboxamidopropenonitrile **3b** was obtained and elucidated on the basis of IR, ^1H NMR and elemental analyses data.

The dienic character of both **3a** and **3b** was investigated through their reaction with each of acrylonitrile, ethyl acrylate **4a,b** and N-aryl-maleimides **6a-c** as dienophiles. Thus, each of **3a,b** reacted with excess amount of acrylonitrile (**4a**) under reflux to afford the corresponding cycloadducts **5a,b**. The IR of each of **5a,b** showed the bands of CN and NH_2 groups and their ^1H NMR spectra revealed the signals of thiopyran H-2, H-3, H-4 in addition to aromatic and NH_2 protons. On the other hand their mass spectra gave m/z=291 which agreed with a molecular weight of a molecular formula $C_{17}H_{13}N_3S$ of the assigned structure (cf. Chart 1). Similarly, each of **3a,b** reacted with refluxing ethyl acrylate (**4b**) to afford the corresponding thiopyrans **5c,d** whose structures were elucidated on the basis of IR, ^1H NMR and elemental analyses data. On the other hand, their mass spectra gave m/z=338 which agreed with a molecular weight of a molecular

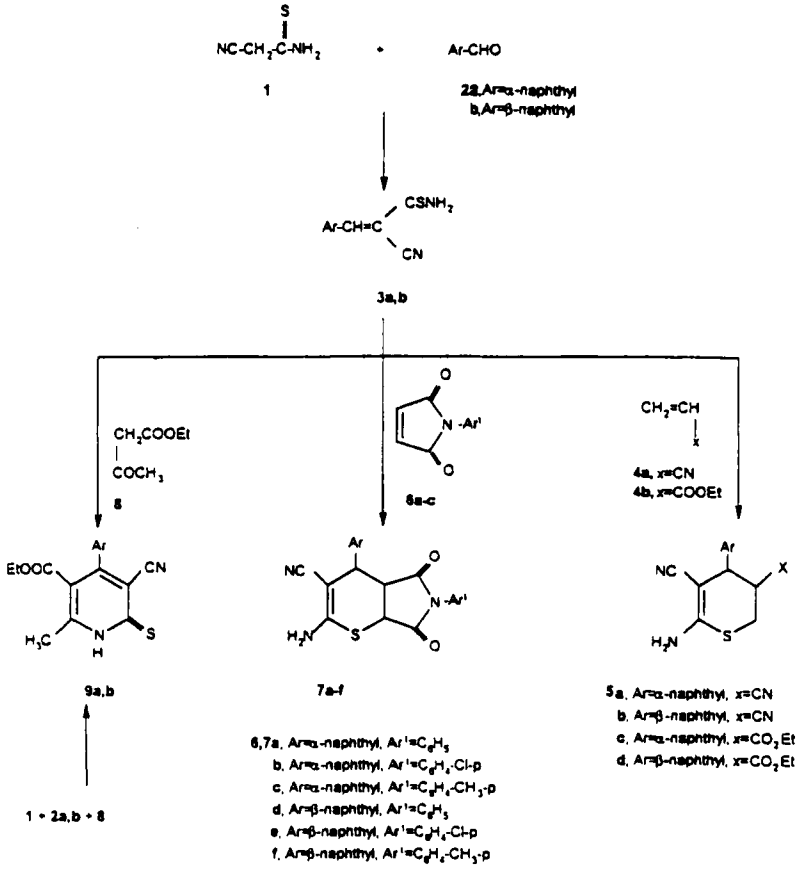

CHART I

formula $C_{19}H_{18}N_2O_2S$ of the assigned structure (cf. Chart 1, Tables I and II). Compound **3a** reacted with N-phenylmaleimide (**6a**), N-(p-chloro)-phenylmaleimide (**6b**)and N-(p-tolyl)-maleimide (**6c**) in an oil bath to afford the corresponding cycloadducts **7a-c** respectively. The IR spectrum of each of **7a-c** showed the bands of NH_2, CN and CO-NAr-CO-groups and their ^1H NMR spectra revealed the signals of NH_2, aromatic, thiopyran H-2, H-3 and H-4 protons (cf. Table II). Moreover, their mass spectra gave m/z=411, 445 and 425 which agreed with the molecular weights of the molecular formulas $C_{24}H_{17}N_3O_2S$, $C_{24}H_{16}N_3O_2SCl$ and $C_{25}H_{19}N_3O_2S$ of the assigned structures (cf. Chart 1, Tables I and II). In a

similar way compound **3b** reacted with each of **6a-c** to give the corresponding cycloadducts **7d-f** whose structures were established by considering the data of IR, ^{1}H NMR and elemental analyses (cf. Tables I and II).

Work was extended to shed more light on the reactivity of **3a,b**. Thus, each of **3a,b** reacted with ethyl acetoacetate (**8**) in refluxing ethanol containing a catalytic amount of piperidine to afford the corresponding pyridinethione derivatives **9a,b** in a respective manner. The IR, ^{1}H NMR and elemental analyses data are the basis on which **9a,b** structures were confirmed (cf. Tables I and II). Moreover, the mass spectra of each of **9a,b** gave m/z=348 which corresponding to the molecular weight of a molecular formula $C_{20}H_{16}N_2O_2S$ of the assigned structure (cf. Chart 1). Further confirmation of **9a,b** structure was performed via the preparation of their authentic samples through the reaction of a ternary mixture of **1, 8** and each of **2a,b**. It is remarkable to report here that **9a,b** synthesized by the two ways are identical in all physical and chemical properties. Furthermore, pyridinethione derivative **9a** reacted with each of ω-bromoacetophenone derivatives **10a-c** in refluxing ethanol containing 10% KOH (≈ 10 ml) to afford the corresponding thieno[2,3-b]pyridine derivatives **12a-c** respectively. Compounds **12a-c** were formed most probably via the non-isolable intermediates **11a-c** respectively through the dehydrobromination reaction. Other analogue **9b** reacted under similar experimental conditions to give the corresponding thieno[2,3-b]pyridine derivatives **12d-f** through the non-isolable products **11d-f**. Structures of **12a-f** were elucidated on the basis of IR, ^{1}H NMR and elemental analyses data (cf. Tables I and II). Moreover, the mass spectra of **12a,c,e** as selective examples gave m/z=466, 480 and 500 which agreed with the molecular weights of the formulas $C_{28}H_{22}N_2O_3S$, $C_{29}H_{24}N_2O_3S$ and $C_{28}H_{21}N_2O_3SCl$ of the assigned structures (cf. Chart 2).

Synthons **9a,b** reacted with chloroacetamide (**13**) in refluxing methanolic sodium methoxide to afford the corresponding 2-S-acetamidopyridine derivatives **14a,b** respectively whose structures were elucidated by considering the data of IR, ^{1}H NMR and elemental analyses (cf. Tables I and II). Further confirmation of **14a,b** structures arose from their cyclization in refluxing ethanol containing 10% KOH (≈ 10 ml) to give the corresponding thieno[2,3-b]pyridine derivatives **15a,b** respectively. Compound **15b** reacted with cold and stirred solution of sodium nitrite and concentrated hydrochloricacid to give the corresponding pyridothienotriazine derivative **16b**. The isolation of **16b** in good and pure state represented as

a good evidence of **15b** structure. Also, compounds **15a,b** cyclized with acetic anhydride, formic acid and reacted with carbon disulfide in refluxing pyridine to afford the corresponding pyridothienopyrimidine derivatives **17a,b, 19a,b and 18a,b** respectively. All structures of **16–19** were confirmed by considering the data tabulated in Table I and II.

TABLE I Characterization data of the newly synthesized compounds

Comp.	*M.P. (°C) (Colour)*	*Yield (%)*	*Molecular Formula*	*% Analysis Calcd./Found*				
				C	*H*	*N*	*S*	*Cl*
3a	188	91	$C_{14}H_{10}N_2S$	70.58	4.20	11.76	13.44	----
	Yellow			70.6	4.4	11.6	13.5	----
3b	168	75	$C_{14}H_{10}N_2S$	70.58	4.20	11.76	13.44	----
	Red			70.2	4.0	11.5	13.1	----
5a	230	86	$C_{17}H_{13}N_3S$	70.10	4.46	14.43	10.99	----
	White			70.2	4.5	14.6	11.1	----
5b	250	89	$C_{17}H_{13}N_3S$	70.10	4.46	14.43	10.99	----
	White			70.3	4.6	14.2	10.7	----
5c	238	76	$C_{19}H_{18}N_2O_2S$	67.45	5.32	8.28	9.46	----
	White			67.7	5.2	8.5	9.5	----
5d	268	76	$C_{19}H_{18}N_2O_2S$	67.45	5.32	8.28	9.46	----
	White			67.5	5.5	8.4	9.6	----
7a	244	89	$C_{24}H_{17}N_3O_2S$	70.07	4.13	10.21	7.78	----
	Pale brown			70.2	4.3	10.5	7.6	----
7b	266	90	$C_{24}H_{16}N_3O_2SCl$	64.64	3.59	9.42	7.18	7.96
	White			64.8	3.8	9.6	7.4	7.8
7c	236	92	$C_{25}H_{19}N_3O_2S$	70.58	4.47	9.88	7.52	----
	White			70.3	4.2	9.7	7.4	----
7d	258	87	$C_{24}H_{17}N_3O_2S$	70.07	4.13	10.21	7.78	----
	Pale brown			70.3	4.4	10.0	7.6	----
7e	224	91	$C_{24}H_{16}N_3O_2SCl$	64.64	3.59	9.42	7.18	7.96
	White			64.5	3.3	9.2	7.3	7.7
7f	276	89	$C_{25}H_{19}N_3O_2S$	70.58	4.47	9.88	7.52	----
	Brown			70.7	4.6	9.5	7.7	----
9a	242	88	$C_{20}H_{16}N_2O_2S$	68.96	4.59	8.04	9.19	----
	Yellow			68.8	4.6	8.2	9.2	----
9b	234	81	$C_{20}H_{16}N_2O_2S$	68.96	4.59	8.04	9.19	----

Comp.	M.P. (°C) (Colour)	Yield (%)	Molecular Formula	% Analysis Calcd./Found				
				C	H	N	S	Cl
	Yellow			68.7	4.3	8.0	9.3	----
12a	188	82	$C_{28}H_{22}N_2O_3S$	72.10	4.72	6.00	6.86	----
	Yellow			72.3	4.7	6.2	6.6	----
12b	158	88	$C_{28}H_{21}N_2O_3SCl$	67.13	4.19	5.59	6.39	7.09
	Yellow			67.3	4.3	5.7	6.2	7.0
12c	172	75	$C_{29}H_{24}N_2O_3S$	72.50	5.00	5.83	6.66	----
	Yellow			72.6	4.9	5.9	6.7	----
12d	184	87	$C_{28}H_{22}N_2O_3S$	72.10	4.72	6.00	6.86	----
	Yellow			72.3	4.6	6.3	6.9	----
12e	154	88	$C_{28}H_{21}N_2O_3SCl$	67.13	4.19	5.59	6.39	7.09
	Orange			67.2	4.3	5.4	6.4	7.1
12f	178	68	$C_{29}H_{24}N_2O_3S$	72.50	5.00	5.83	6.66	----
	Yellow			72.3	4.9	6.1	6.7	----
14a	186	79	$C_{22}H_{19}N_3O_3S$	65.18	4.69	10.37	7.90	----
	Yellow			65.3	4.4	10.5	7.6	-----
14b	170	90	$C_{22}H_{19}N_3O_3S$	65.18	4.69	10.37	7.90	----
	Yellow			65.3	4.6	10.5	8.0	----
15a	236	75	$C_{22}H_{19}N_3O_3S$	65.18	4.69	10.37	7.90	----
	Yellow			65.0	4.6	10.4	7.7	----
15b	210	75	$C_{22}H_{19}N_3O_3S$	65.18	4.69	10.37	7.90	----
	Yellow			65.3	4.5	10.5	7.8	----
16b	222	81	$C_{22}H_{16}N_4O_3S$	63.46	3.84	13.46	7.69	----
	White			63.6	3.6	13.5	7.7	----
17a	>350	52	$C_{24}H_{19}N_3O_3S$	67.13	4.42	9.79	7.45	----
	White			67.0	4.4	9.8	7.3	----
17b	334	58	$C_{24}H_{19}N_3O_3S$	67.13	4.42	9.79	7.45	----
	White			67.3	4.6	9.7	7.5	----
18a	298	73	$C_{23}H_{17}N_3O_3S_2$	61.74	3.80	9.39	14.31	----
	Brown			61.9	4.1	9.2	14.2	----
18b	278	78	$C_{23}H_{17}N_3O_3S_2$	61.74	3.80	9.39	14.31	----
	Buff			61.6	3.7	9.1	14.4	----
19a	288	88	$C_{23}H_{17}N_3O_3S$	66.50	4.09	10.12	7.71	----
	White			66.8	4.1	9.8	7.5	----

Comp.	M.P. (°C) (Colour)	Yield (%)	Molecular Formula	% Analysis Calcd./Found				
				C	H	N	S	Cl
19b	276	88	$C_{23}H_{17}N_3O_3S$	66.50	4.09	10.12	7.71	----
	White			66.2	4.0	9.9	7.5	----

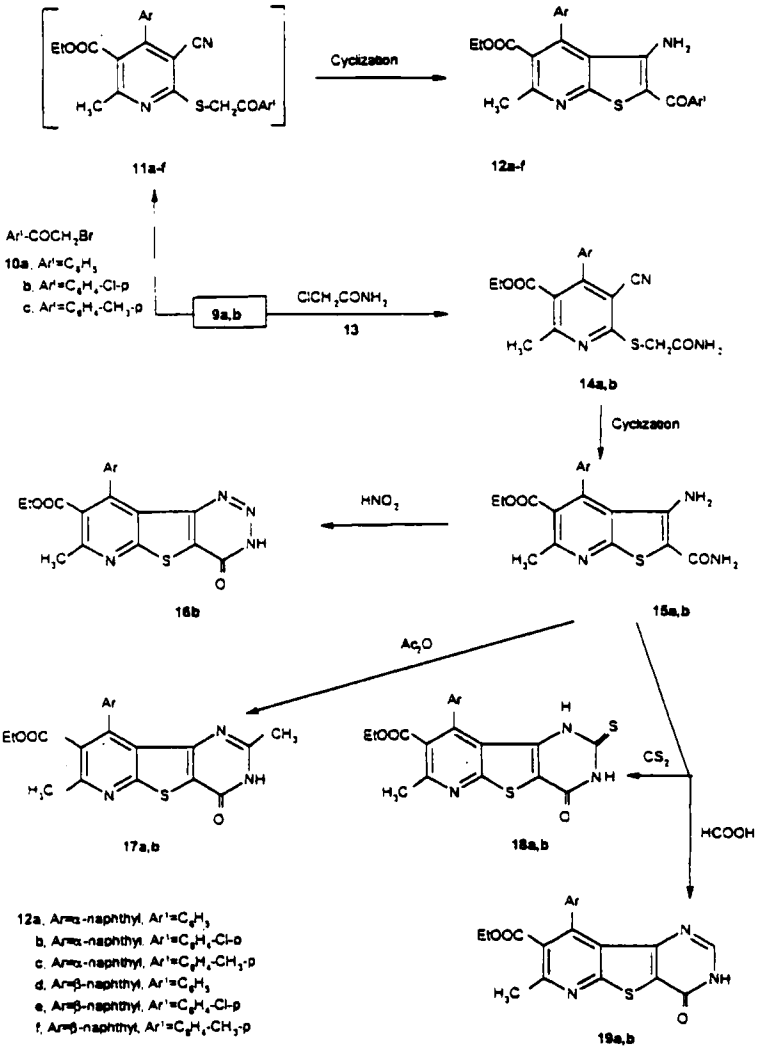

CHART 2

TABLE II IR and ^{1}H NMR data

Comp.	*IR [KBr, cm^{-1}]*	*^{1}H NMR [δ ppm]*
3a	3340, 3265 (NH_2); 3115 (CH aromatic) and 2212 (CN).	5.3 (s, br., 2H, NH_2) and 7.5–8.6 (m, 8H, vinylic and ArH's)
3b	3342, 3271 (NH_2); 3170 (CH aromatic) and 2209 (CN).	
5a	3416, 3283 (NH_2); 3091 (CH aromatic); 2971 (CH sat.) and 2229 (CN).	
5b	3403, 3276 (NH_2); 3077 (CH aromatic); 2977 (CH sat.) and 2225 (CN).	
5c	3375, 3263 (NH_2); 3053 (CH aromatic); 2979 (CH sat.); 2229 (CN) 1719 (CO-ester).	0.9 (t, 3H, CH_2CH_3); 3.5 (q, 2H, CH_2CH_3); 3.6 (q, 1H, -CH-COOEt); 4.2 (d, 1H, -CH-Ar); 4.6 (d, 2H, -S-CH_2-); 6.3 (s, br., 2H, NH_2) and 7.0–7.9 (m, 7H, ArH's).
5d	3381, 3282 (NH_2); 3047 (CH aromatic); 2971 (CH sat.); 2225 (CN) 1721 (CO-ester).	1.1 (t, 3H, CH_2CH_3); 2.8 (d, 1H, -CH- Ar); 3.7 (q, 2H, CH_2CH_3) 3.9 (q, 1H, -CH-COOEt); 5.2 (d, 2H, -S-CH_2-); 4.6 (s, br., 2H, NH_2) and 7.0–7.8 (m, 7H, ArH's).
7a	3413, 3303 (NH_2); 3039 (CH aromatic); 2969 (CH sat.); 2227 (CN) 1711, 1779 (CO-NAr-CO).	3.9 (d, 1H, thiopyran H-3); 4.3 (t, 1H, thiopyran H-4); 4.7 (d, 1H, thiopyran H-2); 6.3 (s, br., 2H, NH_2) and 7.0–7.9 (m, 12H, ArH's).
7b	3411, 3298 (NH_2); 3067 (CH aromatic); 2977 (CH sat.); 2225 (CN) 1711, 1779 (CO-NAr-CO).	
7c	3409, 3315 (NH_2); 3048 (CH 22 aromatic); 2966 (CH sat.); 2221 (CN) 1711, 1779 (CO-NAr-CO).	
7d	3397, 3315 (NH_2); 3041 (CH aromatic); 2976 (CH sat.); 2219 (CN) 1711, 1779 (CO-NAr-CO).	
7e	3421, 3310 (NH_2); 3059 (CH aromatic); 2979 (CH sat.); 2224. (CN) 1711, 1779 (CO-NAr-CO).	

Comp.	*IR [KBr, cm^{-1}]*	*^1H NMR [δ ppm]*
7f	3402, 3311 (NH_2); 3041 (CH aromatic); 2969 (CH sat.); 2223 (CN) 1711, 1779 (CO-NAr-CO).	
9a	3224 (NH); 3102 (CH aromatic); 2981(CH sat.); 2228 (CN) and 1718 (CO- ester).	
9b	3166 (NH); 3058 (CH aromatic); 2973, 2864 (CH sat.); 2230 (CN) and 1710 (CO-ester).	
12a	3462, 3279 (NH_2); 3042 (CH aromatic); 2975 (CH sat.) and 1705 (CO-ester).	
12b	3462, 3268 (NH_2); 3046 (CH aromatic); 2977 (CH sat.) and 1705 (CO-ester).	
12c	3476, 3321 (NH_2); 3054 (CH aromatic); 2975 (CH sat.) and 1708 (CO-ester).	0.4 (t, 3H, $CH_2\mathbf{CH_3}$); 2.8 (s, 3H, CH_3); 2.4 (s, 3H, phenyl-CH_3) 3.8 (q, 2H, $\mathbf{CH_2}CH_3$); 6.3 (s, br., 2H, NH_2) and 7.2–8.1 (m, 11H, ArH's).
12d	3460, 3310 (NH_2); 3050 (CH aromatic); 2970 (CH sat.) and 1718 (CO-ester).	
12e	3468, 3298 (NH_2); 3040 (CH aromatic); 2981 (CH sat.) and 1721 (CO-ester).	
12f	3465, 3302 (NH_2); 3043 (CH aromatic); 2980 (CH sat.) and 1724 (CO-ester).	
14a	3415, 3296 (NH_2); 3044 (CH aromatic); 2967 (CH sat.); 2219 (CN); 1720 (CO-ester) and 1679 (CO-amidic).	0.6 (t, 3H, $CH_2\mathbf{CH_3}$); 2.6 (s, 3H, CH_3); 4.0 (s, 2H, CH_2) 3.7 (q, 2H, $\mathbf{CH_2}CH_3$); 5.6 (s, br., 2H, NH_2) and 7.3–7.9 (m, 7H, ArH's).
14b	3413, 3272 (NH_2); 3056 (CH aromatic); 2973 (CH sat.); 2222 (CN); 1722 (CO-ester) and 1679 (CO-amidic).	
15a	3466, 3319, 3263 (two NH_2); 3168 (CH aromatic); 2976 (CH sat.); 1718 (CO-ester) and 1654 (CO-amidic).	

Comp.	*IR [KBr; cm^{-1}]*	*^1H NMR [δ ppm]*
15b	3465, 3319, 3262 (two NH_2); 3162 (CH aromatic); 2976 (CH sat.); 1718 (CO-ester) and 1654 (CO-amidic).	0.7 (t, 3H, CH_2CH_3); 3.7 (s, 3H, CH_3); 3.9 (q, 2H, CH_2CH_3); 5.6 and 6.7 (s, br., 4H, two NH_2) and 7.2–8.0 (m, 7H, ArH's).
16b	3232 (NH); 3057 (CH aromatic); 2979 (CH sat.); 1710 (CO-ester) and 1687 (CO-amidic).	
17a	3377 (NH); 2998 (CH aromatic); 2922 (CH sat.); 1719 (CO-ester) and 1658 (CO-amidic).	
17b	3439 (NH); 2974 (CH aromatic); 2922 (CH sat.); 1718 (CO-ester) and 1651 (CO-amidic).	
18a	3338, 3225 (two NH); 3011 (CH aromatic); 2982 (CH sat.); 1714 (CO-ester) and 1662 (CO-amidic).	
18b	3312, 3223 (two NH); 3027 (CH aromatic); 2973 (CH sat.); 1722 (CO-ester) and 1669 (CO-amidic).	0.7 (t, 3H, CH_2CH_3); 2.6 (s, 3H, CH_3); 3.7 (q, 2H, CH_2CH_3); 5.5 and 5.7 (s, br., 2H, two NH) and 7.1–8.0 (m, 7H, ArH's).
19a	3261 (NH); 3037 (CH aromatic); 2967 (CH sat.); 1709 (CO-ester) and 1673 (CO-amidic).	0.7 (t, 3H, CH_2CH_3); 2.3 (s, 1H, CH=C); 2.9 (s, 3H, CH_3); 4.0 (q, 2H, CH_2CH_3); 5.5 (s, br., 1H, NH) and 7.2–8.0 (m, 7H, ArH's).
19b	3250 (NH); 3034 (CH aromatic); 2971 (CH sat.); 1713 (CO-ester) and 1663 (CO-amidic).	

It is remarkable to report here that **11a-f** could not be isolated while **14a-f** were isolated and this is due to the difference in electronic character of both the NH_2 in **13** and the phenyl nucleus in **10a-c**.

EXPERIMENTAL

All melting points are uncorrected. I.R. (KBr disc) were recorded on Pye-Unicam SP-1100 spectrophotometer. ^1H NMR spectra were recorded on Varian EM 390 MHz. Gemini-200 MHz. and Brucker WP-80 spectrometers using TMS as an internal standard and $CDCl_3$, DMSO-d_6 and $(CD_3)_2CO$ as solvents and chemical shifts are expressed as ppm units. Mass spectra were recorded on Hewlett-Packard GC-MS type 2988 using inlet type at 70 ev. Microanalyses were performed by the Microanalytical center of Cairo University.

General method for preparation of 3a,b

A solution of **2a,b** (0.01mole) and cyanothioacetamide (**1**) (0.01 mole) in absolute ethanol (30 mL) and the catalytic amount of piperidine (0.3 mL) was stirred at room temperature until solid products obtained which were collected by filtration, washed with ethanol, dried then crystallized from ethanol to give **3a,b** respectively.

General method for preparation of thiopyran derivatives 5a-d

A mixture of **3a,b** (0.01mole) and the excess amounts of **4a,b** is heated under reflux for 3–4 hours. The reaction mixture was evaporated till dryness then diluted with few drops of water. The products so formed were collected by filtration, washed with ethanol and then recrystallized from ethanol to give **5a-d** respectively.

General method for preparation of 7a-f

A mixture of **3a,b** and **6a-c** (0.01 mole of each) was fused with each other and heated in an oil bath for 1 hour. The reaction mixture was cooled and triturated with acetic acid. The product so formed was collected by filtra-

tion, washed with coled diluted acetic acid and then crystallized from acetic acid to give **7a-f** respectively.

Synthesis of 3-cyano-4-aryl-5-ethoxycarbonyl-6-methyl-2-pyridinethione derivatives 9a,b

Method (A)

A solution of **3a,b** and ethyl acetoacetate (**8**) (0.01mole of each) in absolute ethanol (30 mL) containing the catalytic amount of piperidine (0.4 mL) was heated under reflux for 5 hours. The reaction mixture was then evaporated till dryness and then cooled. The product so formed was collected by filtration, washed with cold ethanol and then crystallized from ethanol to give **9a,b** respectively.

Method (B)

A solution of ternary mixture of **1, 2a,b** and ethyl acetoacetae (**8**) (0.01mole of each) in absolute ethanol (30 mL) containing a catalytic amount of piperidine (0.4 mL) was refluxed for 5 hours. The reaction mixture was then evaporated till dryness and then cooled. The product so formed was collected by filtration, washed with cold ethanol and then crystallized from ethanol to give **9a,b** respectively.

Synthesis of 2-S-acetamidopyridine derivatives 14a,b

A mixture of **9a,b** and chloroacetamide (**13**, 0.01mole of each), in methanol containing sodium methoxide (prepared by 0.01 atom Na in methanol) was refluxed for 3 hours. The reaction mixture was then evaporated till dryness and then cooled. The product so formed was collected by filtration, washed with cold ethanol and then crystallized from ethanol to give **14a,b** respectively.

Synthesis of thieno[2,3-b]pyridines 12a-f and 15a,b:(General method)

A solution of **9a,b** with **10a-c** and **14a,b** (0.01 mole of each) in ethanol containing KOH 10% (10 mL) was refluxed for 1–2 hours. The reaction mixture was then evaporated till dryness and then cooled. The product so

formed was collected by filtration, washed with cold ethanol and then crystallized from ethanol to give **12a-f** and **15a,b** respectively.

Synthesis of pyridothienotriazine derivative 16b

To a cold solution of **15b** in ethanol and hydrochloric acid (0.01mole of each) was added a cold aqueous sodium nitrite solution (0.01 mole) drop wisely with stirring, after complete addition of sodium nitrite, stirring was continued for 2–3 hours in ice bath. The product so formed was collected by filtration, washed with cold water and then ethanol and crystallized from ethanol to give **16b**.

Synthesis of pyridothienopyrimidinones 17a,b and 19a,b

(General method)

A Solution of **15a,b** (0.01 mole) in acetic anhydride or formic acid was refluxed for 3 hours. The reaction mixtures were cooled and the products so formed were collected by filtration, washed with cold ethanol and then crystallized from ethanol to give **17a,b** and **19a,b** respectively.

Synthesis of pyridothienopyrimidinones 18a,b

(General method)

A solution of **15a,b** and carbon disulfide (0.01 mole of each) in pyridine (50 mL) was refluxed for 5 hours. The reaction mixture was cooled, then poured onto ice-cold water. The product so formed was collected by filtration, washed with cold water and then ethanol and crystallized from ethanol to give **18a,b** respectively.

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