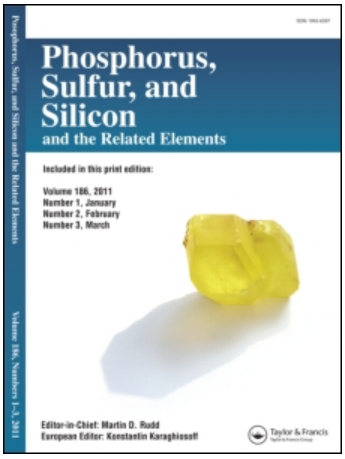

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Cyanothioacetamide and Its Derivatives in Heterocyclic Chemistry: Synthesis of Some New Thioxopyridine, Thienopyridine, and Pyridothienopyrimidine Derivatives

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Cyanothioacetamide and Its Derivatives in Heterocyclic Chemistry: Synthesis of Some New Thioxopyridine, Thienopyridine, and Pyridothienopyrimidine Derivatives

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*A number of thieno[2,3-*b*]pyridines (**9–13**) and pyridothienopyrimidines (**14–16**) were synthesized via the reaction of the dihydrothioxopyridine derivatives (**7a,b**), obtained by the action of ethyl acetoacetate on arylidine cyanothioacetamide **4**, with halogenated compounds **8a–f**.*

Keywords Cyanothioacetamide; dihydrothioxopyridine; pyridothienopyrimidine; thienopyridine

INTRODUCTION

Much effort has been done in the synthesis of heterocyclic compounds using cyanothioacetamide and its derivatives.[1–10] Many thienopyridine derivatives obtained by this route have been evaluated to possess good antibacterial,[11–13] antihypertensive,[14] antimicrobial,[15] analgesic, and anti-inflamatory[16–18] activities, and to act as gonadotropin-releasing hormone antagonists.[17,18] Pyridothienopyrimidines are known to exhibit analgesic and anti-inflammatory activities.[19] These findings along with our interest in the synthesis of thienopyridines[5,20] via the reaction of cyanoacetamide with aldehydes and dicarbonyl derivatives prompted us to attempt the synthesis of new representatives of these heterocycles using cyanothioacetamide with new aromatic aldehyde derivatives.

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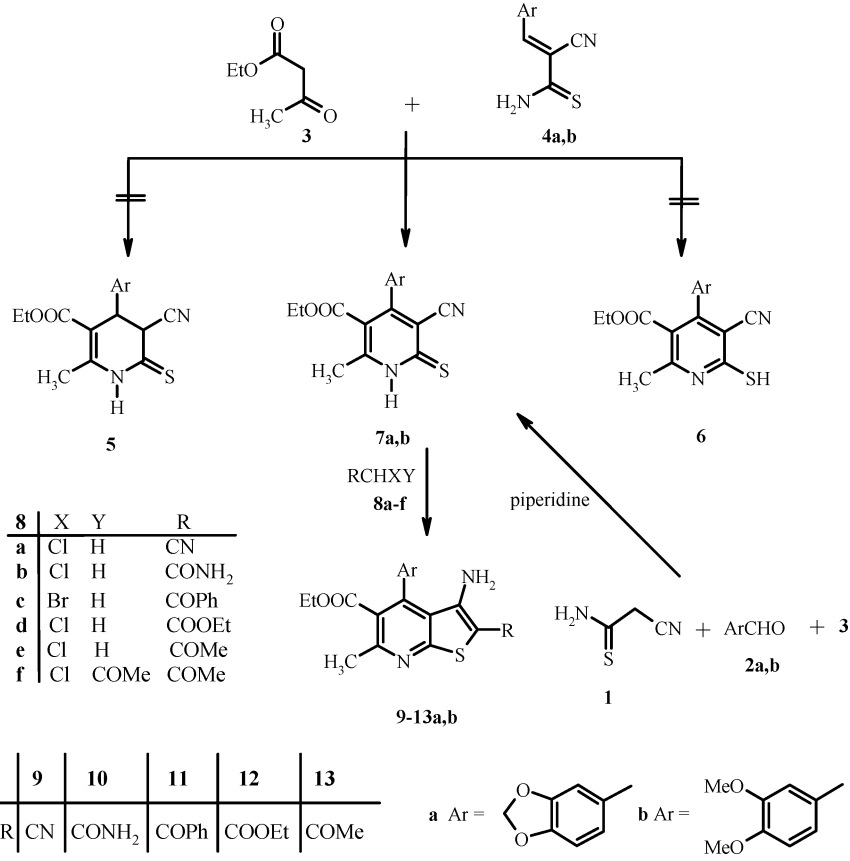
RESULTS AND DISCUSSION

Here we report the synthesis of some new thienopyridines and pyridothienopyrimidines beginning with dihydrothioxopyridine derivatives **7a**,**b**. Compounds **7a**,**b** were prepared in a one-pot reaction of cyanothioacetamide **1**, aromatic aldehydes **2a**,**b**, and ethyl acetoacetate **3** under reflux conditions in dioxane containing a catalytic amount of piperidine, or from the reaction of the arylidene cyanothioacetamides **4a**,**b** with ethyl acetate under the same reaction conditions. The structures of the compounds **7a**,**b** result from correct analytical and spectroscopic data (Tables I and II). Compounds **5**[21] or **6**[5] were not detected among the reaction products (Scheme 1).

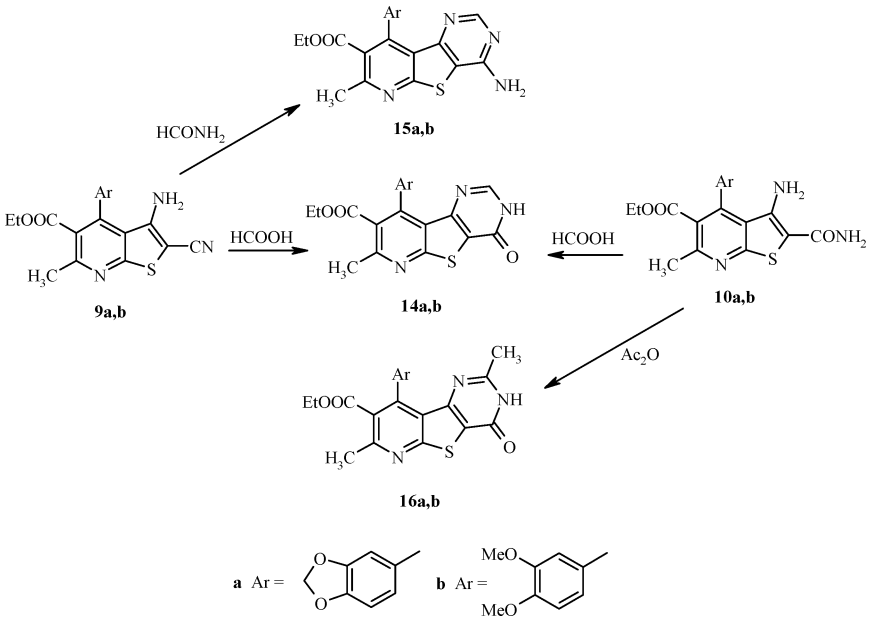


8	X	Y	R
a	Cl	H	CN
b	Cl	H	$CONH_2$
c	Br	H	COPh
d	Cl	H	COOEt
e	Cl	H	COMe
f	Cl	COMe	COMe

	9	10	11	12	13
R	CN	$CONH_2$	COPh	COOEt	COMe

SCHEME 1

Treatment of compounds **7a**,**b** with halogenated compounds **8a–f** in basic ethanolic solution under reflux conditions gave the thieno[2,3-*b*]pyridine derivatives **9a**,**b through 13a**,**b** (Scheme 2). The structures of compounds **9–13** were assigned on the basis of elemental analyses and spectroscopic data. The IR spectra of all compounds reveal the absence of NH and CN absorption bands, typical for **7a**,**b**, and showabsorption bands of NH_2 in addition to new bands corresponding to the introduced new substituents. The ^1H NMR spectrum of **12a** (Table I) shows a new broad signal at $\delta = 5.75$ ppm, which is assigned to the NH_2 protons. The products from the reaction of **7a**,**b** with **8e** proved to be identical in all respects (melting points, IR, ^1H, and ^{13}C NMR, mass spectra) with those obtained from **7a**,**b** and **8f**.



SCHEME 2

The structures of compounds **9a,b** and **10a,b** were further confirmed by the following reactions: treatment of compounds **9a,b** or **10a,b** with formic acid, of **9a,b** with formamide, and of **10a,b** with acetic anhydride at reflux conditions gave the corresponding pyrido[3,2:4,5]thieno[3,2-*d*]pyrimidine derivatives **14a,b through 16a,b,** respectively. The structures of **14–16** are supported by the elemental analyses and the spectroscopic data (Tables I and II). The IR spectrum of **16b** exhibits an

TABLE I Physical Data and Elemental Analyses for Compounds 7, 9–16

Comp.	M.p. (°C) (Color)	Yield (%)	Molecular Formula MS, m^+/z	Analysis Calcd./Found (%) C	H	N	S
7a	245–7	61	$C_{17}H_{14}N_2O_4S$	59.57	4.11	8.17	9.33
	Yellow		356	59.70	4.20	8.10	9.24
7b	226–8	70	$C_{18}H_{18}N_2O_4S$	60.03	5.06	7.81	8.92
	Yellow		372	60.12	4.96	7.78	8.87
9a	258–60	89	$C_{19}H_{15}N_3O_4S$	59.83	3.96	11.02	8.39
	Yellow		381	59.69	3.78	10.89	8.31
9b	248–50	78	$C_{20}H_{19}N_3O_4S$	60.44	4.81	10.57	8.05
	Yellow		397	60.35	4.78	10.46	8.12
10a	264–6	93	$C_{19}H_{17}N_3O_5S$	57.13	4.29	10.52	8.01
	Yellow		399	57.30	4.18	10.38	7.97
10b	226–4	88	$C_{20}H_{21}N_3O_5S$	57.82	5.09	10.11	7.70
	Yellow		415	57.69	4.97	10.07	7.68
11a	158–60	89	$C_{25}H_{20}N_2O_5S$	65.21	4.37	6.08	6.95
	Yellow		460	65.16	4.29	6.05	6.91
11b	201–3	90	$C_{26}H_{24}N_2O_5S$	65.53	5.07	5.88	6.71
	Yellow		476	65.49	5.04	5.82	6.67
12a	161–3	68	$C_{21}H_{20}N_2O_6S$	58.87	4.70	6.54	7.46
	Yellow		428	58.69	4.65	6.48	7.38
12b	156–8	73	$C_{22}H_{24}N_2O_6S$	59.45	5.44	6.30	7.20
	Yellow		444	59.39	5.36	6.24	7.24
13a	174–6	61	$C_{20}H_{18}N_2O_5S$	60.29	4.55	7.03	8.03
	Yellow		398	60.18	4.47	6.97	8.08
13b	189–91	63	$C_{21}H_{22}N_2O_5S$	60.86	5.35	6.76	7.72
	Orange		414	60.78	5.26	6.69	7.69
14a	288–90	92	$C_{20}H_{15}N_3O_5S$	58.67	3.69	10.26	7.81
	Yellow		409	58.55	3.58	10.19	7.78
14b	268–70	78	$C_{21}H_{19}N_3O_5S$	59.28	4.50	9.88	7.52
	Yellow		425	59.26	4.48	9.80	7.48
15a	244–6	57	$C_{20}H_{16}N_4O_4S$	58.81	3.94	13.72	7.83
	Green		408	58.66	3.78	13.67	7.75
15b	221–3	54	$C_{21}H_{20}N_4O_4S$	59.42	4.75	13.20	7.53
	Green		424	59.34	4.57	13.22	7.50
16a	318–20	55	$C_{21}H_{17}N_3O_5S$	59.57	4.04	9.92	7.55
	White		423	59.48	3.92	9.86	7.51
16b	287–9	50	$C_{22}H_{21}N_3O_5S$	60.12	4.81	9.56	7.28
	White		439	60.08	4.77	9.50	7.19

absorption band at 3160 cm^{-1}, which can be assigned to the NH group. The ^1H NMR spectrum displays a new singlet at $\delta = 2.14$ ppm. The mass spectra of all new compounds were in accord with the assigned structures.

TABLE II IR and NMR Spectroscopic Data of Compounds 7, 9–16

	IR [KBr, cm^{-1}]	^1H NMR [δ, ppm]	^{13}C NMR [δ, ppm]
7a	3458 (NH), 2226 (CN), 1708 (CO)	0.94 (t, $J = 7.2$ Hz, 3H, $COOCH_2\mathbf{CH}_3$), 3.28 (s, 3H, CH_3 pyridine), 3.93 (q, $J = 7.2$ Hz, 2H, $COO\mathbf{CH}_2CH_3$), 6.10 (s, 2H, (OCH_2O)), 6.78-7.03 (m, 3H, arom-H), 13.9 (s, br, 1H, NH)	178.6 (C=S), 164.6 (CO ester), 154.5, 152.6, 148.6, 147.2, 128.7, 121.9, 118.9, 116.4, 114.3, 108.5, 108.2 (C-arom, CN), 101.8 (OCH_2O), 61.5 ($\mathbf{C}H_2CH_3$), 18.0 ($\mathbf{C}H_3$ pyridine), 13.5 ($CH_2\mathbf{C}H_3$)
7b	3446 (NH), 2227 (CN), 1708 (CO ester)	0.96 (t, $J = 7.2$ Hz, 3H, $COOCH_2\mathbf{CH}_3$), 3.15 (s, 3H, CH_3 pyridine), 3.77 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 3.93 (q, $J = 7.2$ Hz, 2H, $COO\mathbf{CH}_2CH_3$), 6.89–7.12 (m, 3H, arom-H), 14.10 (s, br, 1H, NH)	178.5 (C=S), 163.8 (CO ester), 154.4, 152.5, 148.6, 147.3, 128.8, 122.0, 119.1, 116.4, 114.3, 108.5, 108.2 (C-arom, CN), 61.5 ($\mathbf{C}H_2CH_3$), 55.7 (OCH_3), 55.6 (OCH_3), 18.1 ($\mathbf{C}H_3$ pyridine), 13.5 ($CH_2\mathbf{C}H_3$)
9a	3465, 3342 (NH_2), 2197 (CN), 1724 (CO ester)	0.98 (t, $J = 7.2$ Hz, 3H, $COOCH_2\mathbf{CH}_3$), 2.46 (s, 3H, CH_3 pyridine), 4.05 (q, $J = 7.2$ Hz, 2H, $COO\mathbf{CH}_2CH_3$), 5.49 (s, 2H, NH_2), 6.89–7.13 (m, 3H, arom-H)	166.2 (CO ester), 159.6, 157.8, 148.8, 148.7, 145.3, 141.2, 137.9, 136.2, 127.1, 126.4, 124.7, 115.4, 109.6, 108.7 (C- arom, CN), 101.7 (OCH_2O), 62.0 ($\mathbf{C}H_2CH_3$), 24.3 (CH_3 pyridine), 13.9 ($CH_2\mathbf{C}H_3$)
9b	3469, 3346 (NH_2), 2198 (CN), 1728 (CO ester)	0.92 (t, $J = 7.2$ Hz, 3H, $COOCH_2\mathbf{CH}_3$), 2.58 (s, 3H, CH_3 pyridine), 3.75 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 4.01 (q, $J = 7.2$ Hz, 2H, $COO\mathbf{CH}_2CH_3$), 5.57 (s, 2H, NH_2), 6.90–7.14 (m, 3H, arom-H)	166.2 (CO ester), 159.6, 157.6, 148.6, 148.0, 145.4, 140.9, 138.1, 136.4, 127.2, 126.5, 124.9, 115.4, 109.5, 108.7 (C- arom, CN), 62.0 ($\mathbf{C}H_2CH_3$), 55.7 (OCH_3), 55.6 (OCH_3), 18.4 (CH_3 pyridine), 13.9 ($CH_2\mathbf{C}H_3$)
10a	3451, 3325, 3267, 3160 (NH_2), 1724 (CO ester), 1658 (CO amide)	0.98 (t, $J = 7.2$ Hz, 3H, $COOCH_2\mathbf{CH}_3$), 2.48 (s, 3H, CH_3 pyridine), 4.06 (q, $J = 7.2$ Hz, 2H, $COO\mathbf{CH}_2CH_3$), 5.82 (s, 2H, NH_2), 6.13 (s, 2H, OCH_2O), 6.79–6.95 (m, 3H, arom-H), 7.16 (s, br, 2H, NH_2)	167.0 (CO amide), 165.3 (CO ester), 159.4, 153.6, 148.4, 147.6, 146.0, 141.9, 134.4, 126.5, 123.1, 120.4, 109.6, 108.6, 97.9 (C-arom), 101.3 (OCH_2O), 62.5 ($\mathbf{C}H_2CH_3$), 24.3 (CH_3 pyridine), 13.9 ($CH_2\mathbf{C}H_3$)

(Continued on next page)

TABLE II IR and NMR Spectroscopic Data of Compounds 7, 9–16 *(Continued)*

	IR [KBr, cm^{-1}]	^1H NMR [δ, ppm]	^{13}C NMR [δ, ppm]
10b	3480, 3428, 3328, 3266 (NH_2), 1733 (CO ester), 1658 (CO amide)	0.98 (t, $J = 7.2$ Hz, 3H, $COOCH_2\mathbf{CH}_3$), 2.48 (s, 3H, CH_3 pyridine), 3.75 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 4.06 (q, $J =$ 7.2 Hz, 2H, $COO\mathbf{CH}_2CH_3$), 5.82 (s, 2H, NH_2), 6.78-7.05 (m, 3H, arom-H), 7.14 (s, br, 2H, NH_2)	166.8 (CO amide), 165.3 (CO ester), 159.4, 153.7, 148.3, 147.5, 146.1, 141.6, 134.4, 126.8, 123.5, 119.6, 109.9, 108.6, 97.9 (C arom), 55.8 (OCH_3), 55.7 (OCH_3), 62.5 ($\mathbf{C}H_2CH_3$), 24.3 (CH_3 pyridine), 13.9 ($CH_2\mathbf{C}H_3$)
11a	3464, 3320 (NH_2), 1728 (CO ester)	0.98 (t, $J = 7.2$ Hz, 3H, $COOCH_2\mathbf{CH}_3$), 2.58 (s, 3H, CH_3 pyridine), 4.06 (q, $J = 7.2$ Hz, 2H, $COO\mathbf{CH}_2CH_3$), 6.15 (s, 2H, OCH_2O), 6.85–7.76 (m, 10H, arom-H, NH_2)	196.5 (CO ketone), 166.2 (CO ester), 160.2, 156.4, 148.8, 148.5, 146.3, 141.1, 135.6, 133.7, 132.7, 128.3, 128.0, 126.5, 125.7, 120.4, 118.3, 109.3, 107.0 (C-arom), 101.8 (OCH_2O), 62.1 ($\mathbf{C}H_2CH_3$), 24.3 (CH_3 pyridine), 13.8 ($CH_2\mathbf{C}H_3$)
11b	3471, 3325 (NH_2), 1731 (CO ester)	0.93 (t, $J = 7.2$ Hz, 3H, $COOCH_2\mathbf{CH}_3$), 2.57 (s, 3H, CH_3 pyridine), 3.77 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 4.03 (q, $J =$ 7.2 Hz, 2H, $COO\mathbf{CH}_2CH_3$), 6.90-7.74 (m, 10H, arom-H, NH_2)	195.8 (CO ketone), 165.6 (CO ester), 160.0, 156.2, 148.8, 148.6, 146.1, 141.2, 137.8, 133.7, 132.9, 128.4, 127.9, 126.2, 125.8, 120.3, 118.4, 109.2.2, 108.0 (C-arom), 61.9 ($\mathbf{C}H_2CH_3$), 55.9 (OCH_3), 55.2 (OCH_3), 24.3 (CH_3 pyridine), 13.8 ($CH_2\mathbf{C}H_3$)
12a	3467, 3345 (NH_2), 1729, 1669 (CO ester)	0.96 (t, $J = 7.2$ Hz, 3H, $COOCH_2\mathbf{CH}_3$), 1.24 (t, $J = 6.9$ Hz, 3H, $COOCH_2\mathbf{CH}_3$), 2.56 (s, 3H, CH_3 pyridine), 4.06 (q, $J = 7.2$ Hz, 2H, $COO\mathbf{CH}_2CH_3$), 4.23 (q, $J = 6.9$ Hz, 2H, $COO\mathbf{CH}_2CH_3$), 6.12 (s, 2H, OCH_2O), 5.75 (s, br, 2H, NH_2), 6.81-7.08 (m, 3H, arom-H)	165.3 (CO ester), 164.2 (CO ester), 159.8, 154.3, 148.4, 147.9, 147.8, 142.4, 134.5, 126.2, 123.0, 119.6, 109.5, 108.8, 94.5 (C-arom), 101.6 (OCH_2O), 62.1 ($\mathbf{C}H_2CH_3$), 61.8 ($\mathbf{C}H_2CH_3$), 24.3 (CH_3pyridine), 14.4 ($CH_2\mathbf{C}H_3$), 13.8 ($CH_2\mathbf{C}H_3$)

(Continued on next page)

TABLE II IR and NMR Spectroscopic Data of Compounds 7, 9–16 *(Continued)*

	IR [KBr, cm^{-1}]	^1H NMR [δ, ppm]	^{13}C NMR [δ, ppm]
12b	3460, 3340 (NH_2), 1735, 1690 (two CO ester)	1.01 (t, $J = 7.2$ Hz, 3H, $COOCH_2\mathbf{CH}_3$), 1.23 (t, $J = 6.9$ Hz, 3H, $COOCH_2\mathbf{CH}_3$), 2.55 (s, 3H, CH_3 pyridine), 3.77 (s, 3H, OCH_3) , 3.83 (s, 3H, OCH_3), 4.04 (q, $J = 7.2$ Hz, 2H, $COO\mathbf{CH}_2CH_3$), 4.22 (q, $J = 6.9$ Hz, $COO\mathbf{CH}_2CH_3$), 5.77 (s, br, 2H, NH_2), 6.84-7.09 (m, 3H, arom-H)	166.1 (CO ester), 164.5 (CO ester), 159.8, 156.3, 148.5, 147.8, 147.7, 142.8, 136.7, 126.8, 125.6, 119.5, 108.9, 108.7, 94.6 (C-arom), 62.1 ($\mathbf{C}H_2CH_3$), 61.8 ($\mathbf{C}H_2CH_3$), 55.2 (OCH_3), 55.8 (OCH_3), 24.3 (CH_3 pyridine), 14.4 ($CH_2\mathbf{C}H_3$), 13.8 ($CH_2\mathbf{C}H_3$)
13a	3472, 3312 (NH_2), 1727 (CO ester)	0.96 (t, $J = 7.2$ Hz, 3H, $COOCH_2\mathbf{CH}_3$), 2.31 (s, 3H, $COCH_3$), 2.55 (s, 3H, CH_3 pyridine), 4.05 (q, $J = 7.2$ Hz, 2H, $COO\mathbf{CH}_2CH_3$), 6.11 (s, 2H, OCH_2O), 6.41 (s, br, 2H, NH_2), 6.80–7.08 (m, 3H, arom-H)	191.7 (CO ketone), 165.9 (CO ester), 159.7, 157.0, 149.1, 148.9, 145.1, 143.2, 134.5, 126.4, 123.8, 119.4, 109.4, 108.8, 104.8 (C-arom), 101.0 (OCH_2O), 61.6 ($\mathbf{C}H_2CH_3$), 29.2 (CH_3 acetyl), 24.3 (CH_3 pyridine), 13.8 ($CH_2\mathbf{C}H_3$)
13b	3465, 3310 (NH_2), 1725 (CO ester)	0.98 (t, $J = 7.2$ Hz, 3H, $COOCH_2\mathbf{CH}_3$), 2.33 (s, 3H, $COCH_3$), 2.54 (s, 3H, CH_3 pyridine), 4.06 (q, $J = 7.2$ Hz, 2H, $COO\mathbf{CH}_2CH_3$), 6.11 (s, 2H, OCH_2O), 6.42 (s, br, 2H, NH_2), 6.83–7.09 (m, 3H, arom-H)	192.2 (CO acetyl), 166.2 (CO ester), 159.3, 155.2, 148.6, 148.2, 145.9, 143.1, 134.6, 126.0, 122.9, 119.6, 109.3, 108.9, 104.7 (C-arom), 61.6 ($\mathbf{C}H_2CH_3$), 55.2 (OCH_3), 55.9 (OCH_3), 29.0 (CH_3 acetyl), 24.3 (CH_3 pyridine), 13.8 ($CH_2\mathbf{C}H_3$)
14a	3159 (NH), 1726 (CO ester), 1669 (CO lactam)	0.99 (t, $J = 7.2$ Hz, 3H, $COOCH_2\mathbf{CH}_3$), 2.62 (s, 3H, CH_3 pyridine), 4.07 (q, $J = 7.2$ Hz, 2H, $COO\mathbf{CH}_2CH_3$), 6.13 (s, 2H, OCH_2O), 6.75–6.98 (m, 3H, arom-H), 8.09 (s, 1H, CH pyrimidine), 12.34 (s, br, 1H, NH)	166.4 (CO ester), 163.5 (CO lactam), 158.6, 157.9, 154.8, 148.9, 147.9, 143.0, 138.5, 135.9, 127.1, 124.5, 119.5, 113.2, 108.3, 106.6 (C-arom), 101.2 (OCH_2O), 61.3 ($\mathbf{C}H_2CH_3$), 24.3 (CH_3 pyridine), 13.9 ($CH_2\mathbf{C}H_3$)

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TABLE II IR and NMR Spectroscopic Data of Compounds 7, 9–16 *(Continued)*

	IR [KBr, cm^{-1}]	^1H NMR [δ, ppm]	^{13}C NMR [δ, ppm]
14b	3166 (NH), 1726 (CO ester), 1645 (CO lactam)	0.96 (t, $J = 7.2$ Hz, 3H, $COOCH_2\mathbf{CH}_3$), 2.62 (s, 3H, CH_3 pyridine), 3.72 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 4.07 (q, $J = 7.2$ Hz, 2H, $COO\mathbf{CH}_2CH_3$), 6.83-7.01 (m, 3H, arom-H), 8.08 (s, 1H, CH pyrimidine), 12.82 (s, 1H, NH)	166.2 (CO ester), 163.9 (CO lactam), 158.4, 157.1, 154.8, 148.9, 147.8, 142.9, 138.7, 135.8, 126.8, 124.4, 120.8, 113.9, 108.3, 106.6 (C-arom), 61.3 ($\mathbf{C}H_2CH_3$), 55.9 (OCH_3), 55.8 (OCH_3), 24.3 (CH_3 pyridine), 13.7 ($CH_2\mathbf{C}H_3$)
15a	3335, 3190 (NH_2), 1725 (CO ester)	1.01 (t, $J = 7.2$ Hz, 3H, $COOCH_2\mathbf{CH}_3$), 2.61 (s, 3H, CH_3 pyridine), 4.08 (q, $J = 7.2$ Hz, 2H, $COO\mathbf{CH}_2CH_3$), 6.14 (s, 2H, OCH_2O), 6.85-7.12 (m, 3H, arom-H), 7.96 (s, 1H, CH pyrimidine), 8.89 (s, br, 2H, NH_2)	169.0 (CO ester), 161.2, 153.9, 152.2, 150.1, 148.7, 146.9, 143.6, 141.8, 140.9, 132.9, 126.7, 125.1, 118.8, 109.7, 107.9 (C arom), 101.2 (OCH_2O), 61.7 ($\mathbf{C}H_2CH_3$), 24.3 (CH_3 pyridine), 13.9 ($CH_2\mathbf{C}H_3$)
15b	3332, 3187 (NH_2), 1717 (CO ester)	0.96 (t, $J = 7.2$ Hz, 3H, $COOCH_2\mathbf{CH}_3$), 2.66 (s, 3H, CH_3 pyrimidine), 3.70 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 4.06 (q, $J = 7.2$ Hz, 2H, $COO\mathbf{CH}_2CH_3$), 6.83-7.01 (m, 3H, arom-H), 8.08 (s, 1H, CH pyrimidine), 8.90 (s, 2H, NH_2)	169.1 (CO ester), 161.1, 154.9, 152.1, 149.9, 148.5, 146.7, 143.6, 141.3, 140.8, 132.7, 126.5, 125.2, 118.7, 109.7, 107.9 (C-arom), 61.7 ($\mathbf{C}H_2CH_3$), 55.9 (OCH_3), 55.7 (OCH_3), 24.3 (CH_3 pyridine), 13.8 ($CH_2\mathbf{C}H_3$)
16a	3163 (NH), 1722 (CO ester), 1658 (CO lactam)	0.98 (t, $J = 7.2$ Hz, 3H, $COOCH_2\mathbf{CH}_3$), 2.13 (s, 3H, CH_3 pyrimidine), 2.61 (s, 3H, CH_3 pyridine), 4.05 (q, $J = 7.2$ Hz, 2H, $COO\mathbf{CH}_2CH_3$), 6.13 (s, 2H, OCH_2O), 6.84–7.03 (m, 3H, arom-H), 12.69 (s, 1H, NH)	166.3 (CO ester), 163.2 (CO lactam), 162.3, 158.1, 156.7, 154.4, 149.7, 141.3, 137.8, 135.7, 127.1, 124.4, 119.5, 113.3, 112.3, 106.7 (C-arom), 101.2 (OCH_2O), 61.3 ($\mathbf{C}H_2CH_3$), 24.3 (CH_3 pyridine), 21.9 (CH_3 pyrimidinone), 13.9 ($CH_2\mathbf{C}H_3$)

(Continued on next page)

TABLE II IR and NMR Spectroscopic Data of Compounds 7, 9–16 *(Continued)*

	IR [KBr, cm^{-1}]	^1H NMR [δ, ppm]	^{13}C NMR [δ, ppm]
16b	3160 (NH), 1720 (CO ester), 1655 (CO lactam)	0.97 (t, $J = 7.2$ Hz, 3H, $COOCH_2\mathbf{CH}_3$), 2.14 (s, 3H, CH_3 pyrimidine), 2.62 (s, 3H, CH_3 pyridine), 3.72 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 4.06 (q, $J = 7.2$ Hz, 2H, $COO\mathbf{CH}_2CH_3$), 6.83–7.02 (m, 3H, arom-H), 12.71 (s, 1H, NH)	166.4 (CO ester), 164.0 (CO lactam), 163.3, 158.2, 156.9, 154.6, 151.8, 142.8, 140.6, 138.2, 126.9, 124.4, 120.3, 113.8, 112.3, 108.4 (C-arom), 61.3 ($\mathbf{C}H_2CH_3$), 55.8 (OCH_3), 55.7 (OCH_3), 24.3 (CH_3 pyridine), 22.9 (CH_3 pyrimidinone), 13.7 ($CH_2\mathbf{C}H_3$)

EXPERIMENTAL

The melting points were determined on an electrothermal melting point apparatus and are uncorrected. IR spectra were recorded on a Pye Unicam SP 3-300 and a Shimadzu FT IR 8101 PC IR spectrophotometer (KBr pellets). ^1H and ^{13}C NMR spectra were recorded on a Varian Mercury VX-300 MHz NMR spectrometer in DMSO-d_6 solution using TMS as an internal reference. Electron impact mass spectra were obtained with a 70 eV Shimadzu GCMS-QP 1000 EX spectrometer. Elemental analyses were carried out at the Microanalytical Center at Cairo University, Giza, Egypt. The arylidine cyanothioacetamides **4a**,**b**[22,23] were prepared as previously reported.

Synthesis of Thioxo-1,6-dihydropyridine-3-carboxylates (7a,b)

Method A

A mixture of **4a**,**b** (0.01 mol) and ethyl acetoacetate (1.3 g, 0.01 mol) in dioxane (30 mL) containing a catalytic amount of piperidine (0.3 mL) was refluxed for 4 h. The solvent of the reaction mixture was evaporated. The solid formed was collected by filtration, washed with ethanol (15 mL), and crystallized from ethanol to give the respective thioxopyridine **7**.

Method B

A mixture of cyanothioacetamide (0.01 mol), ethyl acetoacetate (0.01 mol), and the respective aromatic aldehyde (0.01 mol) in dioxane (30 mL) containing a catalytic amount of piperidine (0.3 mL) was heated

at reflux for 5 h. The solvent of the reaction mixture was evaporated, and the crude product was collected, washed with ethanol (15 mL), and crystallized from ethanol to give compounds **7a,b**.

Synthesis of 3-Amino-6-methylthieno [2,3-*b*]pyridine-5-carboxylates (9a,b–13a,b)

A solution of **7a,b** (0.01 mol) in ethanol (50 mL) containing 10% potassium hydroxide was treated with **8a–f** (0.01 mol) and refluxed for 3 h. After cooling the reaction mixture was poured in ice-cold water (50 mL). The solid formed was collected, washed with water (20 mL), and crystallized from ethanol to give **9a,b–13a,b**.

Synthesis of Ethyl Pyrido[3,2:4,5]thieno[3,2-*d*]pyrimidine-8-carboxylates (14a,b–16a,b)

A solution of **9a**,**b** or **10a**,**b** (0.01 mol) in an excess of formic acid (30 mL), a solution of **9a**,**b** (0.01 mol) in an excess of formamide (30 mL), or a solution of **10a**,**b** (0.01 mol) in an excess of acetic anhydride (50 mL) was refluxed for 4 h. The reaction mixture was cooled to ambient temperature, and the product formed was collected, washed with cold ethanol (10 mL), and crystallized from ethanol to give the corresponding products **14a**,**b**–**16a**,**b**.

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