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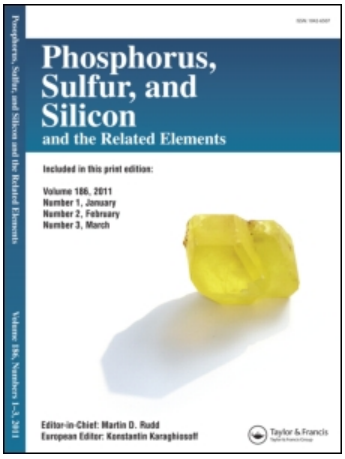

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REACTIONS WITH CYANOTHIOACETAMIDE DERIVATIVES: SYNTHESIS AND REACTIONS OF SOME PYRAZOLO[3,4-*b*]PYRIDINE DERIVATIVES

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To cite this Article Attaby, Fawzy A. , Ibrahim, Laila I. , Eldin, Sanaa M. and El-louh, Ali K. K.(1992) 'REACTIONS WITH CYANOTHIOACETAMIDE DERIVATIVES: SYNTHESIS AND REACTIONS OF SOME PYRAZOLO[3,4-*b*]PYRIDINE DERIVATIVES', Phosphorus, Sulfur, and Silicon and the Related Elements, 73: 1, 127 — 135
To link to this Article: DOI: 10.1080/10426509208034439
URL: http://dx.doi.org/10.1080/10426509208034439

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Phosphorus, Sulfur, and Silicon, 1992, Vol. 73, pp. 127–135
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REACTIONS WITH CYANOTHIOACETAMIDE DERIVATIVES: SYNTHESIS AND REACTIONS OF SOME PYRAZOLO[3,4-*b*]PYRIDINE DERIVATIVES

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(Received April 16, 1992; in final form Aug. 25, 1992)

The ylidene derivatives of cyanothioacetamide 1a–d reacted with ethyl acetoacetate to give the pyridinethiol derivatives 2a–d. Compounds 2a–d were used as starting material for the synthesis of several heterocyclic compounds. Reactions with hydrazine hydrate, ethyl iodide, methyl chloroacetate and α-chloro ethyl acetoacetate gave the pyridine and annelated pyridine derivatives 5a–d, 6a–d, 7a, 8b–d, and 12a–d, respectively. Compounds 7a, 8b–d and 12a–d reacted with hydrazine hydrate to yield the annelated pyridines 10a–d and 15a–d, respectively.

Key words: Cyanothioacetamide; pyridines; thienopyridines; pyrazolopyridines; thieno[4,4]spiropyrazolo[2,3-*b*]pyridines.

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INTRODUCTION

During the last few years our research group has been interested in the chemistry of cyanothioacetamide and its derivatives[1–7] with the objective of finding new routes for the synthesis of heterocyclic derivatives with expected biological activities. The considerable biological activities of pyridine and its annelated derivatives as antimycotic,[8] antidepressant,[9] fungicidal agents,[10] antiarrhythmic[11] and antioipemic[12] agents stimulated our interest in the synthesis of several new derivatives of these ring systems. A. Krauze[13] reported that the thiocarboxamidocinnamonitrile derivatives 1a–d reacted with ethyl acetoacetate to give the 3-cyano-5-ethoxycarbonyl-6-methyl-4-aryltetrahydropyridine-2-thiones 3a–d. In our laboratory, however, the same reaction gave products which were found totally different in melting points and spectral data than those of A. Krauze.[13] These reaction products were thus formulated as the 3-cyano-5-ethoxycarbonyl-6-methyl-4-arylpyridine-2-thiols 2a–d which were taken as the starting for the study.

RESULTS AND DISCUSSION

Thus, it has been found that 2a–d reacted with hydrazine hydrate in a molecular ratio of 1:1 to afford the sulfur-free products 5a–d. The IR spectra of 5a–d showed absorption bands of NH_2, NH, ester CO and C=N groups while those of the cyano

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group were entirely absent. The pyrazolo[3,4-*b*]pyridine derivatives 5a–d were assumed to be formed via the intermediacy of 4a–d.

Compounds 2a–d reacted also with ethyl iodide in aqueous sodium hydroxide solution to give the corresponding 2-mercaptoethyl derivatives 6a–d. Structural elucidation of 6a–d was based on both elemental analysis and spectral data (cf.

TABLE I

Characterization data of the newly synthesized compounds

Comp. (Colour)	M.P. (°C)	Yield (%)	Molecular formula	% Analysis Calcd/Found				
				C	H	N	S	Cl
2a	252	80	$C_{16}H_{14}N_2SO_2$	64.42	4.69	9.39	10.73	—
(Yellow)				64.30	4.60	9.40	10.80	—
2b	220	78	$C_{16}H_{13}N_2SO_2Cl$	57.83	3.91	8.43	9.63	10.54
(Yellow)				57.78	3.85	8.50	9.70	10.50
2c	214	75	$C_{17}H_{16}N_2SO_3$	62.19	4.87	8.53	9.75	—
(Yellow)				62.22	4.80	8.50	9.80	—
2d	200	90	$C_{16}H_{13}N_3SO_4$	55.97	3.79	12.24	9.32	—
(Orange)				56.00	3.82	12.30	9.40	—
5a	255	78	$C_{16}H_{16}N_4O_2$	64.86	5.40	18.91	—	—
(Yellow)				65.00	5.50	19.00	—	—
5b	279	83	$C_{16}H_{15}N_4O_2Cl$	58.18	4.54	16.96	—	10.60
(Yellow)				58.20	4.55	16.90	—	10.80
5c	261	85	$C_{17}H_{18}N_4O_3$	62.57	5.52	17.17	—	—
(Pale yellow)				62.60	5.50	17.20	—	—
5d	277	90	$C_{16}H_{15}N_5O_4$	56.30	4.39	20.52	—	—
(Orange)				56.30	4.40	20.60	—	—
6a	55	90	$C_{18}H_{18}N_2SO_2$	66.25	5.52	8.58	9.81	—
(White)				66.30	5.50	8.60	9.80	—
6b	50	95	$C_{18}H_{17}N_2SO_2Cl$	60.00	4.72	7.77	8.88	9.72
(White)				60.10	4.70	7.70	8.80	9.60
6c	80	90	$C_{19}H_{20}N_2SO_3$	64.06	5.61	7.86	8.98	—
(White)				64.00	5.60	7.80	9.00	—
6d	60	85	$C_{16}H_{17}N_3SO_4$	58.22	4.58	11.32	8.62	—
(Golden yellow)				58.20	4.60	11.30	8.60	—
7a	117	80	$C_{19}H_{18}N_2SO_4$	61.62	4.86	7.56	8.64	—
(Buff)				61.60	4.90	7.60	8.60	—
8b	180	85	$C_{19}H_{17}N_2O_4Cl$	56.43	4.20	6.93	7.92	8.66
(Yellow)				56.40	4.25	6.90	7.90	8.70
8c	162	75	$C_{20}H_{20}N_2SO_5$	60.00	5.00	7.00	8.00	—
(White)				59.90	5.00	6.90	8.10	—
8d	225	90	$C_{19}H_{17}N_3SO_6$	54.93	4.09	10.12	7.71	—
(Yellow)				54.90	4.10	10.09	7.70	—
10a	226	80	$C_{18}H_{15}N_3SO_3$	61.18	4.24	11.89	9.06	—
(Golden yellow)				61.15	4.20	11.90	9.00	—
10b	166	85	$C_{18}N_{14}N_3SO_3Cl$	55.81	3.61	10.85	8.26	9.04
(Yellow)				55.80	3.61	10.90	8.30	9.00
10c	>300	83	$C_{19}H_{17}N_3SO_4$	59.53	4.43	10.96	8.35	—
(Grey)				59.50	4.45	10.92	8.30	—
10d	>300	90	$C_{18}H_{14}N_4SO_5$	54.27	3.51	14.07	8.04	—
(Grey)				54.30	3.50	14.10	8.00	—
12a	128	82	$C_{22}H_{22}H_2SO_5$	61.97	5.16	6.57	7.51	—
(White)				62.00	5.20	6.60	7.70	—
12b	150	80	$C_{22}H_{21}N_2SO_5Cl$	57.39	4.56	6.08	6.95	7.60
(Golden yellow)				57.40	4.54	6.10	6.90	7.60

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TABLE I (*continued*)

Comp. (Colour)	M.P. (°C)	Yield (%)	Molecular formula	% Analysis Calcd/Found				
				C	H	N	S	Cl
12c (Brown)	160	79	$C_{23}H_{24}N_2SO_6$	60.52 60.54	5.26 5.25	6.14 6.20	7.01 7.00	— —
12d (Brown)	170	75	$C_{22}H_{21}N_3S_2SO_7$	56.50 56.09	4.45 4.50	8.91 8.94	6.79 6.70	— —
15a (Yellow)	181	80	$C_{20}H_{18}N_4SO_2$	60.91 60.95	4.56 4.58	14.21 14.27	8.12 8.10	— —
15b (Yellow)	200	90	$C_{20}H_{17}N_4SO_2Cl$	56.07 56.02	3.97 3.99	13.08 13.10	7.47 7.40	8.17 8.30
15c (Orange)	170	79	$C_{21}H_{20}N_4SO_3$	59.43 59.45	4.71 4.74	13.20 13.26	7.54 7.50	— —
15d (Brown)	228	90	$C_{20}H_{17}N_5SO_4$	56.73 56.77	4.01 4.04	16.54 16.55	7.56 7.50	— —

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TABLE II

IR and ^{1}H-NMR spectral data of the newly synthesized compounds

Comp.	IR (cm^{-1})	^{1}H-NMR (δ ppm)
2a	3020 (aromatic CH); 2950 (Sat. CH); 2550 (SH); 2220 (CN); 1730 (CO ester); 1640 (C=N) and 1620 (C=C).	1.1 (t, 3H, CH_3CH_2); 2.3 (s, 3H, CH_3); 3.9 (q, 2H, CH_2CH_3); 7.3–7.8 (m, 5H, phenyl) and 14.1 (s, 1H, SH).
2b	3025 (aromatic CH); 2940 (Sat. CH); 2555 (SH); 2225 (CN); 1735 (CO ester); 1645 (C=N) and 1610 (C=C).	1.1 (t, 3H, CH_3CH_2); 2.2 (s, 3H, CH_3); 3.7 (q, 2H, CH_2CH_3); 7.4–7.8 (m, 4H, ArH's) and 14.2 (s, 1H, SH).
2c	3030 (aromatic CH); 2930 (Sat. CH); 2560 (SH); 2227 (CN); 1730 (CO ester); 1635 (C=N) and 1615 (C=C).	1.0 (t, 3H, (CH_3CH_2); 2.1 (s, 3H, CH_3); 2.9 (s, 3H, OCH_3); 3.9 (q, 2H, CH_2CH_3); 7.3–7.9 (m, 4H, ArH's) and 14.0 (s, 1H, SH).
2d	3020 (aromatic CH); 2950 (Sat. CH); 2550 (SH); 2225 (CN); 1735 (CO ester); 1640 (C=N) and 1628 (C=C).	1.2 (t, 3H, CH_3CH_2); 2.2 (s, 3H); 3.9 (q, 2H, CH_2CH_3); 7.4–7.9 (m, 4H, ArH's) and 14.1 (s, 1H, SH).
5a	3490, 3300 and 3200 (NH_2 and NH); 3070 (aromatic CH); 2950 (Sat. CH); 1730 (CO ester); 1640 (C=N) and 1600 (C=C).	1.2 (t, 3H, CH_3CH_2); 2.3 (s, 3H, CH_3); 3.9 (q, 2H, CH_2CH_3); 4.7 (s, 2H, NH_2); 7.2–7.8 (m, 5H, phenyl) and 12.2 (s, 1H, NH).
5b	3485, 3290 and 3200 (NH_2 and NH); 3060 (aromatic CH); 2950 (Sat. CH); 1735 (CO ester); 1635 (C=N) and 1600 (C=C).	1.1 (t, 3H, CH_3CH_2); 2.3 (s, 3H, CH_3); 3.8 (q, 2H, CH_2CH_3); 4.6 (s, 2H, NH_2); 7.3–7.9 (m, 4H, ArH's) and 12.1 (s, 1H, NH).
5c	3490, 3300 and 3200 (NH_2 and NH); 3050 (aromatic CH); 2950 (Sat. CH); 1735 (CO ester); 1640 (C=N) and 1610 (C=C).	1.2 (t, 3H, CH_3CH_2); 2.3 (s, 3H, CH_3); 3.0 (s, 3H, OCH_3); 3.9 (q, 2H, CH_2CH_3); 4.6 (s, 2H, NH_2); 7.2–7.8 (m, 4H, ArH's) and 12.1 (s, 1H, NH).
5d	3490, 3320 and 3190 (NH_2 and NH); 3030 (aromatic CH); 2950 (Sat. CH); 1730 (CO ester); 1640 (C=N) and 1600 (C=C).	1.2 (t. 3H, CH_3CH_2); 2.4 (s, 3H, CH_3); 3.9 (q, 2H, CH_2CH_3); 4.6 (s, 2H, NH_2); 7.3–7.9 (m, 4H, ArH's) and 12.3 (s, 1H, NH).

TABLE II (*continued*)

Comp.	IR (cm^{-1})	^{1}H-NMR (δ ppm)
6a	3060 (aromatic CH); 2950 (Sat. CH); 2227 (CN); 1735 (CO ester); 1630 (C=N) and 1600 (C=C).	1.2 (t, 6H, two CH_3CH_2); 2.5 (S, 3H, CH_3); 3.9 (q, 4H, two CH_2CH_3) and 7.2–7.8 5H, phenyl).
6b	3070 (aromatic CH); 2940 (Sat. CH); 2225 (CN); 1730 (CO ester); 1640 (C=N) and 1600 (C=C).	1.2 (t, 6H, two CH_3CH_2); 2.3 (s, 3H, CH_3); 3.8 (q, 4H, two CH_2CH_3) and 7.3–7.9 (m, 4H, ArH's).
6c	3050 (aromatic CH); 2950 (Sat. CH); 2220 (CN); 1735 (CO ester); 1640 (C=N) and 1600 (C=C).	1.2 (t, 6H, two CH_3CH_2); 2.3 (s, 3H, CH_3); 3.0 (s, 3H, OCH_3); 3.9 (q, 4H, two CH_2CH_3 and 7.2–7.8 (m, 4H, ArH's).
6d	3070 (aromatic CH); 2960 (Sat. CH); 2227 (CN); 1735 (CO ester); 1640 (C=N) and 1600 (C=C).	1.1 (t, 6H, two CH_3CH_2); 2.3 (s, 3H, CH_3); 3.9 (q, 4H, two CH_2CH_3) and 7.3–8.0 (m, 4H, ArH's).
7a	3060 (aromatic CH); 2950 (Sat. CH); 2225 (CN); 1750 and 1720 (two CO ester); 1640 (C=N) and 1600 (C=C).	1.1 (t, 3H, CH_3CH_2); 2.3 (s, 3H, CH_3 at the 6-position); 3.1 (s, 3H, CH_3OCOCH_2—S—); 3.6 (s, 2H, CH_2COOCH_3); 4.1 (q, 2H, CH_2CH_3) and 7.2–7.9 (m, 5H, ArH's).
8b	3490 and 3380 (NH_2); 3060 (aromatic CH); 3960 (Sat. CH); 1730 and 1690 (two CO ester); 1640 (C=N) and 1600 (C=C).	1.1 (t, 3H, CH_3CH_2); 2.5 (s, 3H CH_3 at the 6-position); 3.3 (s, 3H, CH_3OCO); 4.1 (q, 2H, CH_2CH_3); 5.8 (s, br., 2H, NH_2) and 7.3–7.8 (m, 4H, ArH's).
8c	3490 and 3390 (NH_2); 3070 (aromatic CH); 2940 (Sat. CH); 1730 and 1690 (two CO ester); 1640 (C=N) and 1600 (C=C).	1.1 (t, 3H, CH_3CH_2); 2.3 (s, 3H, CH_3 at the 6-position); 3.0 (s, 3H, OCH_3); 3.8 (s, 3H, CH_3OCO); 4.1 (q, 2H, CH_2CH_3); 5.9 (s, br., 2H, NH_2) and 7.2–7.9 (m, 4H, ArH's).
8d	3490 and 3400 (NH_2); 3060 (aromatic CH); 2960 (Sat. CH); 1735 and 1700 (two CO ester); 160 (C=N) and 1600 (C=C).	1.2 (t, 3H, CH_3CH_2); 2.4 (s, 3H CH_3 at the 6-position); 3.5 (s, 3H, CH_3OCO); 4.2 (q, 2H, CH_2CH_3); 5.8 (s, br., 2H, NH_2) and 7.3–7.9 (m, 4H, ArH's).
10a	3500 (OH); 3380 (NH); 3060 (aromatic CH); 2970 (Sat. CH); 1730 (CO ester); 1645 (C=N) and 1600 (C=C).	1.1 (t, 3H, CH_3CH_2); 2.4 (s, 3H, CH_3 at pyridine ring); 4.0 (q, 2H, CH_2CH_3); 5.9 (s, br., 1H, NH); 7.4–7.8 (m, 5H, phenyl protons) and 12.2 (s, 1H, OH).
10b	3495 (OH); 3390 (NH); 3070 (aromatic CH); 1735 (CO ester); 1645 (C=N) and 1660 (C=C).	1.2 (t, 3H, CH_3CH_2); 2.5 (s, 3H, CH_3 at pyridine ring); 4.1 (q, 2H, CH_2CH_3); 5.9 (s, br., 1H, NH); 7.3–7.8 (m, 4H, ArH's) and 12.1 (s, 1H, OH).
10c	3490 (OH); 3380 (NH); 3060 (aromatic CH); 2960 (Sat. CH); 1730 (CO ester; 1645 (C=N) and 1600 (C=C).	1.1 (t, 3H, CH_3CH_2); 2.4 (s, 3H, CH_3 at pyridine); 2.9 (s, 3H, OCH_3); 4.1 (q, 2H, CH_2CH_3); 6.0 (s, br., 1H, NH); 7.4–7.8 (m, 4H, ArH's) and 12.1 (s, 1H, OH).
10d	3495 (OH); 3385 (NH); 3070 (aromatic CH); 2950 (Sat. CH); 1730 (CO ester); 1640 (C=N) and 1600 (C=C).	1.2 (t, 3H, CH_3CH_2); 2.5 (s, 3H, CH_3 at pyridine); 4.2 (q, 2H, CH_2CH_3); 6.1 (s, br., 1H, NH); 7.5–8.0 (m, 4H, ArH's) and 12.1 (s, 1H, OH).

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TABLE II (*continued*)

Comp.	IR (cm^{-1})	^{1}H-NMR (δ ppm)
12a	3390 (NH); 3070 (aromatic CH); 2950 (Sat. CH); 1735 (CO ester) and 1690 (CO acetyl).	1.1 (t, 3H, CH_3CH_2OCO at pyridine); 1.3 (t, 3H, CH_3CH_2OCO at thiophene); 2.4 (s, 3H, CH_3 at pyridine); 3.2 (s, 3H, CH_3CO); 3.9–4.2 (two overlapped, q, 4H, two CH_2CH_3); 5.7 (s, br., 1H, NH) and 7.3–7.9 (m, 5H, phenyl).
12b	3390 (NH); 3070 (aromatic CH); 2950 (Sat. CH); 1735 (CO ester) and 1690 (CO acetyl).	1.1 (t, 3H, CH_3CH_2OCO at pyridine); 1.3 (t, 3H, CH_3CH_2OCO at thiophene); 3.4 (s, 3H, CH_3CO); 3.8–4.1 (two overlapped, q, 4H, two CH_2CH_3); 5.9 (s, br., 1H, NH) and 7.2–7.8 (m, 4H, Arh's).
12c	3400 (NH); 3070 (aromatic CH); 2950 (Sat. CH); 1740 (CO ester) and 1700 (CO acetyl).	1.1 (t, 3H, CH_3CH_2OCO at pyridine); 1.3 (t, 3H, CH_3CH_2OCO at thiophene); 2.2 (s, 3H, CH_3 at pyridine); 2.9 (s, 3H, OCH_3); 3.5 (s, 3H, CH_3CO); 3.9–4.1 (two overlapped, q, 4H, two CH_2CH_3); 6.0 (s, br., 1H, NH) and 7.3–7.9 (m, 4H, ArH's).
12d	3400 (NH); 3090 (aromatic CH); 2960 (Sat. CH); 1740 (CO ester) and 1700 (CO acetyl).	1.1 (t, 3H, CH_3CH_2OCO at pyridine); 1.3 (t, 3H, CH_3CH_2 at thiophene); 2.4 (s, 3H, CH_3 at pyridine); 3.6 (s, 3H, CH_3CO); 3.9–4.1 (two overlapped, q, 4H, two CH_2CH_3); (s, br., 1H, NH) and 7.4–8.0 (m, 4H, ArH's).
15a	3500 (OH); 3390 (NH); 3060 (aromatic CH); 2960 (Sat. CH); 1735 (CO ester) and 1645 (C=N).	1.1 (t, 3H, CH_3CH_2); 2.4 (s, 3H, CH_3 at pyridine); 3.3 (s, 3H, CH_3 at pyrazole); 4.1 (q, 2H, CH_2CH_3); 5.9 (s, br., 1H, NH); 7.4–7.9 (m, 5H, phenyl) and 9.3 (m, 1H, OH).
15b	3500 (OH); 3390 (NH); 3060 (aromatic CH); 2960 (Sat. CH); 1735 (CO ester) and 1640 (C=N).	1.1 (t, 3H, CH_3CH_2); 2.4 (s, 3H CH_3 at pyridine); 3.3 (s, 3H, CH_3 at pyrazole); 4.0 (q, 2H CH_2CH_3); 5.8 (s, br., 1H, NH), 7.3–7.8 (m, 4H, ArH's) and 9.3 (s, 1H, OH).
15c	3500 (OH); 3400 (NH); 3070 (aromatic CH); 2950 (Sat. CH); 1740 (CO ester), and 1645 (C=N).	1.1 (t, 3H, CH_3CH_2); 2.3 (s, 3H), CH_3 at pyridine); 2.9 (s, 3H, OCH_3); 3.4 (s, 3H, CH_3 at pyrazole); 4.1 (q, 2H, CH_2CH_3); 5.9 (s, br., 1H, NH); 7.4–7.9 (m, 4H ArH's and 9.4 (s, 1H, OH).
15d	3495 (OH); 3395 (NH); 3060 (aromatic CH); 2690 (Sat. CH); 1730 (CO ester) and 1640 (C=N).	1.1 (t, 3H, CH_3CH_2); 2.3 (s, 3H, CH_3 at pyridine); 3.4 (s, 3H, CH_3 at pyrazole); 4.0 (q, 2H, CH_2CH_3); 5.8 (s, br., 1H, NH); 7.4–8.0 (m, 4H, ArH's) and 9.3 (s, 1H, OH).

Tables I and II). In addition, compounds 6a–d reacted with hydrazine hydrate to yield the same 5a–d previously obtained (cf. Chart 1).

Compound 2a and each of 2b–d reacted with methyl chloroacetate to afford 2-methoxycarbonylmethylmercaptopyridine derivative 7a and the thieno[2,3-*b*]pyridine

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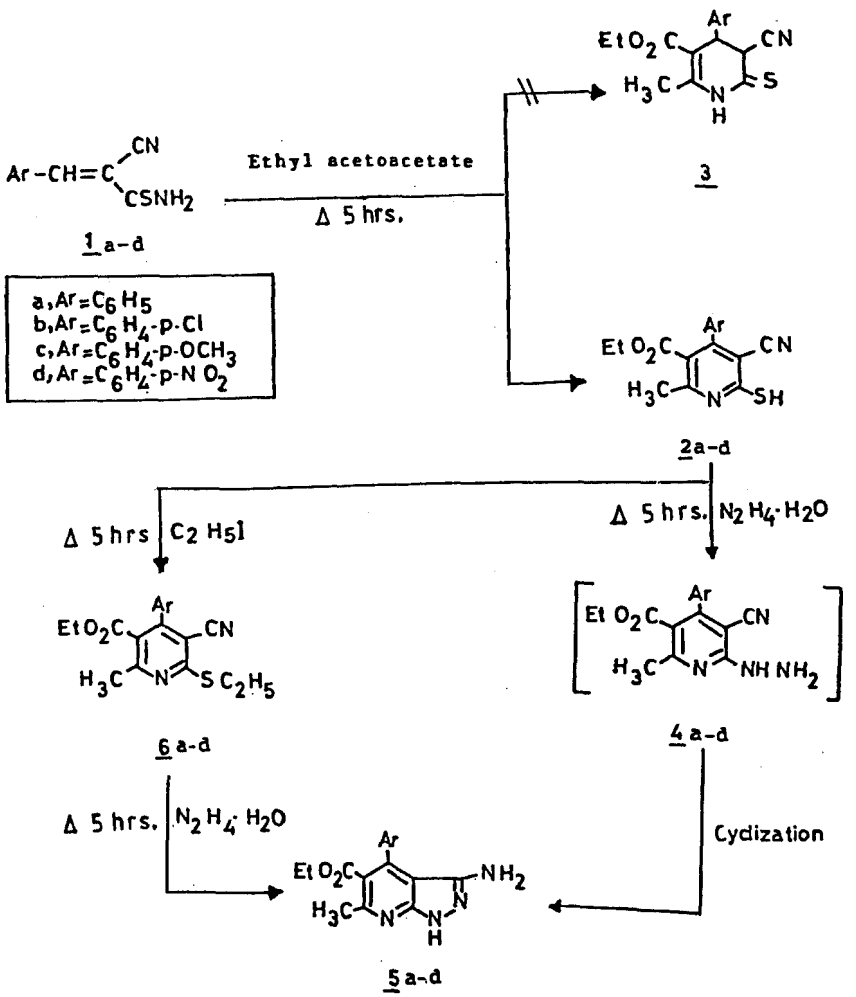

Chart 1

derivatives 8b–d, respectively. Compounds 8b–d were assumed to be formed via the intermediacy of 7b–d. The IR spectrum of 7a showed the absorption bands of the cyano function at 2225 cm^{-1}. The ^1H-NMR spectrum of 7a revealed among its signals that corresponding to the S-CH_2- protons at 3.6 δ ppm.

Attempted cyclisations of 7a into the corresponding 8a were unsuccessful under a variety of reaction conditions. The structure assigned for 8b–d was established based on both elemental analysis and spectral data (cf. Experimental Part). An unequivocal support for the structures of both 7a and 8b–d was achieved via their conversion into the corresponding thieno[3,2-*c*]pyrazolo-[2,3-*b*]pyridine derivatives 10a–d, respectively, by the action of hydrazine hydrate. Compounds 10a–d were assumed to be formed via the intermediacy of 9a–d. The IR spectra of 10a–d showed the presence of absorption bands of enolic OH, NH and CO groups in each case (cf. Experimental Part).

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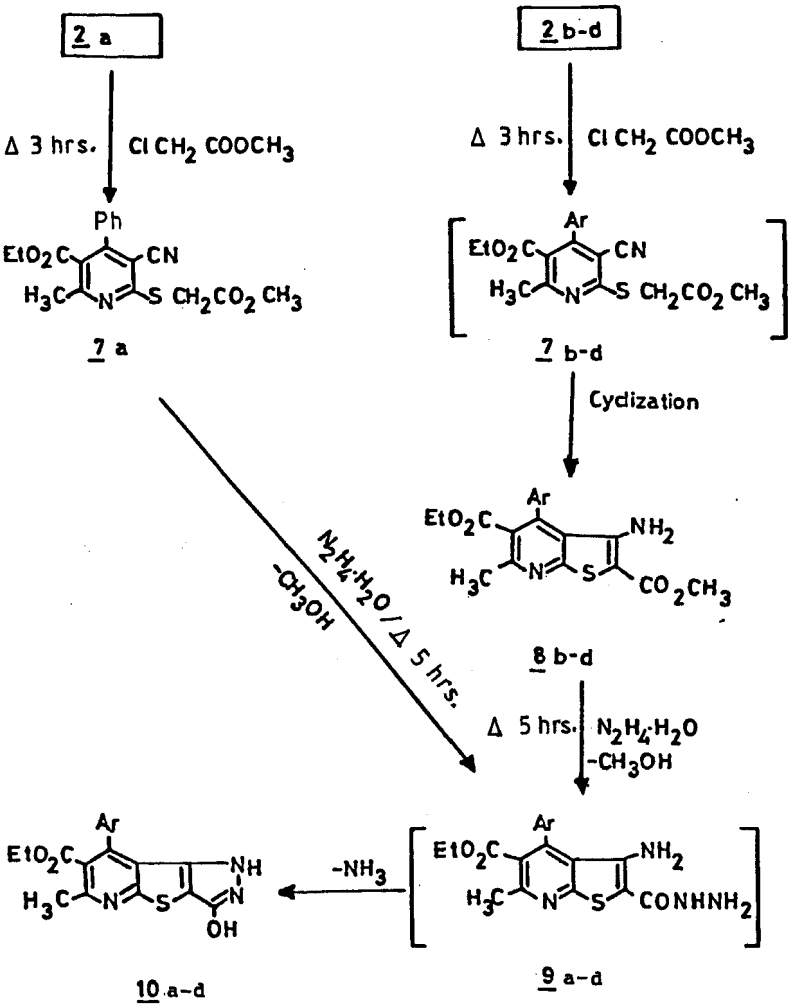

Chart 2

Compounds 2a–d reacted also with ethyl α-chloroacetoacetate to give the thieno[2,3-*b*]pyridine derivatives 12a–d, respectively, via the intermediates 11a–d. The IR spectra of 12a–d showed the presence of NH, ester CO and acetyl CO groups while their ^{1}H-NMR spectra were in a good agreement with the assigned structure (cf. Experimental Part).

Compounds 12a–d reacted, in turn, with hydrazine hydrate to yield the intermediate hydrazones 13a–d. Compounds 13a–d were cyclised under the applied reaction conditions via the loss of ethanol to give the corresponding thieno[4,4]spiropyrazolo[2,3-b]pyridine derivatives 15a–d. The IR and ^{1}H-NMR spectra of 15a–d showed the presence of both OH and NH groups. The above findings excluded structure 14 to represent the products of reaction of 12a–d with hydrazine hydrate (cf. Chart 3).

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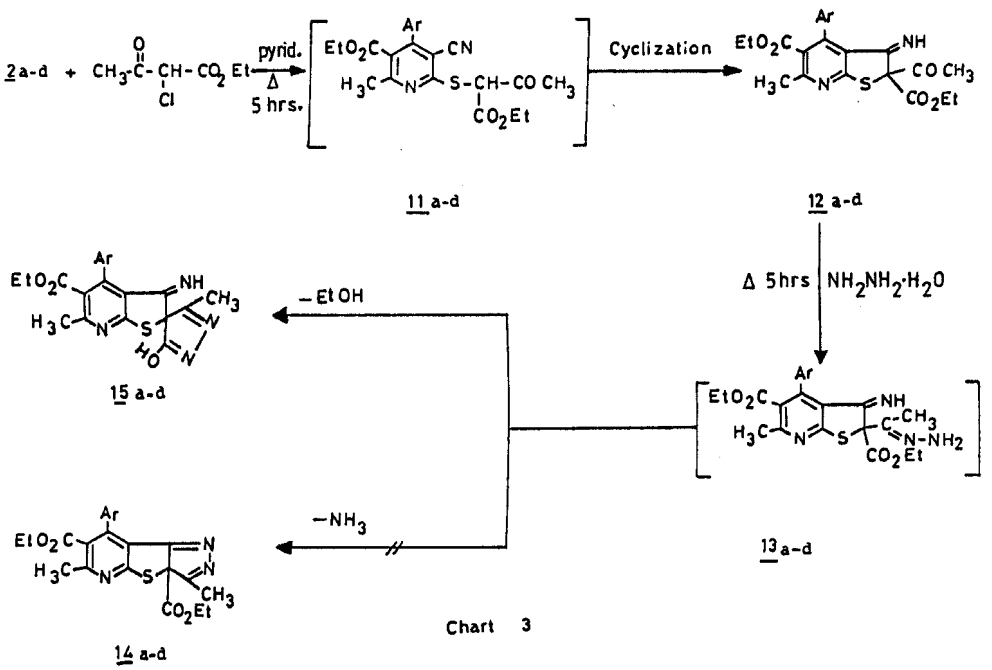

Chart 3

EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded on a Pye-Unicam SP-1100 spectrophotometer using KBr discs. ^{1}H-NMR spectra were recorded on a Varian EM 390 90 MHz and Gemenai 200 MHz spectrometer using DMSO-d_6 as a solvent and TMS as an internal standard. Chemical shifts are expressed as δ ppm units. The microanalyses were performed by the Microanalytical Center of Cairo University using Perkin-Elmer 2400 CHN Elemental Analyzer.

Synthesis of 3-cyano-4-aryl-5-ethoxycarbonyl-6-methylpyridine-2-thiol derivatives 2a–d. A mixture of each of the thiocarboxamidocinnamonitriles (1a–d, 0.01 mol) and ethyl acetoacetate (0.01 mol) in absolute ethanol (50 ml) containing triethylamine (0.5 ml) was heated under reflux for 5 h. The reaction mixture was evaporated till dryness, then cooled and diluted with ice-cold water. The solid product so formed was filtered off and crystallized from ethanol to give 2a–d (cf. Tables I and II).

Synthesis of the 2-ethylmercapto-3-cyano-4-aryl-5-ethoxycarbonyl-6-methylpyridines 6a–d. A mixture of 2a–d (0.01 mol) and ethyl iodide (0.01 mol) in sodium hydroxide (1N, 50 ml) was heated under reflux for 5 h. The reaction mixture was cooled, acidified with conc. HCl and the solid so obtained was filtered off and washed with water. Cyrstallisation from ethanol afforded 6a–d (cf. Tables I and II).

Synthesis of the pyridine derivative 7a *and the thieno[2,3-b]pyridine derivatives* 8b–d: A solution of each of 2a or 2b–d (0.01 mol) and methyl chloroacetate (0.01 mol) in dry acetone (50 ml) containing anhydrous potassium carbonate (2 g) was heated under reflux for 3 h. The reaction mixture was cooled and poured onto cold water. The solid product so formed was filtered off, washed with water and then crystallised from ethanol to give 7a and 8b–d respectively (cf. Tables I and II).

Synthesis of the thieno[2,3-b]pyridines 12a–d: A solution of 12a–d (0.01 mol) and ethyl α-chloroacetoacetate (0.01 mol) in pyridine (30 ml) was heated under reflux for 5 h. Excess of pyridine was removed under reduced pressure. The reaction mixture was poured onto cold water. The solid product thus obtained was filtered off and crystallised from ethanol to give 12a–d (cf. Tables I and II).

Action of hydrazine hydrate on 2a–d, 6a–d, 7a, 8b–d *and* 12a–d: *Synthesis of* 5a–d, 10a, 10b–d *and* 15a–d: *General Procedure.* A solution of each of 2a–d (or 6a–d), 7a, 8b–d and 12a–d (0.01 mol) in absolute ethanol (30 ml) was treated with hydrazine hydrate (0.01 mol) and the reaction mixture was heated under reflux for 5 h. The reaction mixture was evaporated till dryness, cooled and poured onto ice-cold water. The solid product so formed was filtered off and crystallised from ethanol to give 5a–d, 10a, 10b–d and 15a–d, respectively (cf. Tables I and II).

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