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Reactions and Characterization of Pyridin-6-one-2-thione and 3-Diazotized Amino-4-hydroxypyrazolo-[3,4-b]pyridin-6-one

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ABSTRACT: *Several pyrido[2,1-b]thiazines and thiazolo[2,3-a]pyridines were synthesized by reactions of cinnamonitriles with appropriate halocarbonyl compounds. Hydrazones of 3-diazotized aminopyrazolo[3,4-b]pyridinones were synthesized by coupling of their corresponding diazonium salts with several active methylene reagents. The obtained hydrazones were cyclized in refluxing ethanol containing a catalytic amount of triethylamine to afford the corresponding pyrazolopyridotriazines. All structures were established by considering the data of elemental analyses, IR, [1]H-NMR, and mass spectra.* © 1998 John Wiley & Sons, Inc. Heteroatom Chem 9: 571–579, 1998

INTRODUCTION

In the last few years, we have been involved in a program aiming to develop synthetic approaches for polyfunctionally substituted heterocycles using pyridinethiones as starting materials [1–5]. In conjunction with this work, we report novel syntheses of pyrido[2,1-b]thiazines **6a–f;** thiazolo[2,3-a]pyridinones **12, 15a,b, 18,** and **21;** and hydrazones **24a–h** and their fused triazines **25a–h.** Interesting biological activities of these types of compounds have been reported [6–12].

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RESULTS AND DISCUSSION

It has been found that pyridin-6-one-2-thione [13,14] **3** reacts with thiocarboxamidocinnamonitriles **4a–c** in absolute ethanol containing a catalytic amount of triethylamine to afford the compounds **6a–c** through the nonisolable intermediates **5a–c.** The IR spectra of **6a–c** showed the bands of OH, NH_2, CN, and amidic CO groups. Their ^{1}H-NMR spectra revealed the signals of pyridine H-5, thiazine H-4, NH_2, and OH protons. Moreover, the mass spectrum of **6a** as a typical example gave $m/z = 356$, which represents the molecular weight corresponding to molecular formula $C_{16}H_{12}N_4S_2O_2$ of the assigned structure. By consideration of all the foregoing data in addition to elemental analyses, compounds **6a–c** were formulated as pyrido[2,1-b][1,3]thiazin-6(4H)-one derivatives (cf. Tables 1 and 2 and Chart 1).

In a similar manner, compound **3** reacted with carboxamidocinnamonitriles **4d–f** to afford the corresponding pyridothiazines **6d–f,** respectively, whose structures were established based on elemental analyses, IR, and ^{1}H-NMR spectral data (cf. Tables 1 and 2). The synthetic potential of **3** was also investigated with respect to reactions with several halogenated carbonyl compounds. Thus, compound **3** reacted with ethyl chloroacetate (**10a**), chloroacetic acid (**10b**) and chloroacetamide (**10c**) to afford the corresponding 2-S-alkoyl pyridinone derivatives **11a–c** with loss of hydrogen chloride in each case. The structures of **11a–c** were established based on IR and ^{1}H-NMR spectroscopy and on elemental anal-

TABLE 1 Characterization of the Newly Synthesized Compounds

Comp.	M.P. (°C)	Solvent of Cryst.	Yield (%)	Molecular Formula	% of Anal.: Calcd./Found C	H	N	S	Cl
6a	170	ethanol	73	$C_{16}H_{12}N_4S_2O_2$	53.93	3.37	15.73	17.98	—
					54.2	3.6	16.0	18.3	—
6b	190	ethanol	68	$C_{16}H_{11}N_4S_2O_2Cl$	49.17	2.82	14.34	16.39	9.09
					49.4	3.1	14.5	16.6	9.2
6c	250	acetic acid	65	$C_{14}H_{10}N_4S_2O_2$	48.41	3.17	16.14	18.44	—
					48.7	3.5	16.3	18.2	—
6d	>300	DMF	64	$C_{16}H_{12}N_4SO_3$	56.47	3.52	16.47	9.41	—
					56.74	3.8	16.6	9.6	—
6e	195	acetic acid	81	$C_{16}H_{11}N_4SO_3Cl$	51.27	2.94	14.95	8.54	9.48
					51.5	3.2	15.3	8.2	9.6
6f	230	ethanol	72	$C_{14}H_{10}N_4SO_4$	50.91	3.03	16.97	9.70	—
					51.0	3.2	17.2	9.8	—
9	156 dec.	DMF	79	$C_6H_4N_4O_2Cl$	33.72	1.87	32.79	—	16.63
					33.8	1.9	33.0	—	16.7
11a	200	ethanol	64	$C_{10}H_{10}N_2SO_4$	47.24	3.94	11.02	12.60	—
					47.4	4.1	11.3	12.9	—
11b	146	acetic acid	72	$C_8H_6N_2SO_4$	42.48	2.65	12.39	14.16	—
					42.6	2.8	12.6	14.4	—
11c	215	ethanol	62	$C_8H_7N_3SO_3$	42.67	3.11	18.67	14.22	—
					42.9	3.3	18.9	14.5	—
12	>300	DMF	82	$C_8H_4N_2SO_3$	46.15	1.92	13.46	15.38	—
					46.4	2.2	13.1	15.1	—
14a	250	acetic acid	72	$C_8H_8N_2SO_3$	48.21	3.57	12.50	14.29	—
					48.1	3.3	12.8	14.5	—
14b	190	ethanol	65	$C_{11}H_{10}N_2SO_4$	49.62	3.76	10.53	12.03	—
					49.8	3.9	10.2	12.3	—
15a	310	ethanol	69	$C_8H_6N_2SO_2$	52.43	2.91	13.59	15.53	—
					52.1	3.0	13.8	15.7	—
15b	278	acetic acid	75	$C_{11}H_8N_2SO_3$	53.23	3.23	11.29	12.90	—
					53.4	3.5	11.1	13.1	—
17	210	ethanol	69	$C_{14}H_{10}N_2SO_3$	58.74	3.50	9.79	11.19	—
					58.9	3.7	9.5	11.4	—
18	>300	DMF	64	$C_{14}H_8N_2SO_2$	62.69	2.99	10.45	11.94	—
					62.9	3.2	10.2	12.1	—
20	159	ethanol	62	$C_{12}H_{12}N_2SO_4$	48.65	4.05	9.46	10.81	—
					48.8	4.1	9.6	11.0	—
21	>300	DMF	79	$C_{12}H_{10}N_2SO_4$	51.80	3.60	10.07	11.51	—
					51.6	3.7	10.3	11.7	—
24a	175	ethanol	82	$C_{13}H_{15}N_5O_6$	46.29	4.45	20.77	—	—
					46.0	4.6	21.0	—	—
24b	136	ethanol	65	$C_{12}H_{13}N_5O_5$	46.91	4.23	22.80	—	—
					47.1	4.4	23.0	—	—
24c	152	ethanol	73	$C_{11}H_{11}N_5O_4$	47.65	3.97	25.27	—	—
					47.9	4.2	25.5	—	—
24d	179	acetic acid	80	$C_9H_7N_7SO_2$	38.99	2.53	35.38	11.55	—
					39.1	2.3	35.6	11.8	—
24e	192	ethanol	85	$C_9H_7N\text{-}O_2$	41.38	2.68	37.55	—	—
					41.1	2.9	37.8	—	—
24f	148	ethanol	79	$C_{15}H_{10}N_6O_4$	55.90	3.11	26.09	—	—
					56.1	2.9	26.2	—	—
24g	135	ethanol	63	$C_{11}H_{10}N_8O_4$	45.52	3.45	28.97	—	—
					45.8	3.6	29.2	—	—
24h	179	acetic acid	74	$C_{17}H_{15}N_5O_5$	55.28	4.07	18.97	—	—
					55.5	4.3	19.1	—	—
25a	235	ethanol	82	$C_{11}H_8N_5O_5$	45.36	3.09	24.05	—	—
					45.6	3.3	24.2	—	—
25b	197	ethanol	69	$C_{12}H_{11}N_4O_4$	49.83	3.81	24.22	—	—
					49.6	3.6	24.4	—	—
25c	225	ethanol	60	$C_{11}H_8N_4O_3$	50.97	3.48	27.03	—	—
					51.2	3.2	27.2	—	—

TABLE 1 (*Continued*)

Comp.	M.P. (°C)	Solvent of Cryst.	Yield (%)	Molecular Formula	% of Anal.: Calcd./Found C	H	N	S	Cl
25d	258	acetic acid	72	$C_8H_7N\text{-}SO_2$	38.99	2.53	35.38	11.50	—
					39.1	2.8	35.6	11.7	—
25e	305	ethanol	75	$C_9H_7N\text{-}O_3$	41.38	2.68	37.55	—	—
					41.6	2.2	37.8	—	—
25f	278	acetic acid	80	$C_{15}H_{10}N_5O_3$	55.90	3.11	26.59	—	—
					56.1	3.4	26.7	—	—
25g	187	ethanol	69	$C_{11}H_{10}N_6O_4$	45.52	3.45	28.97	—	—
					45.2	3.2	29.1	—	—
25h	289	acetic acid	60	$C_{17}H_{13}N_4O_4$	58.12	3.70	19.94	—	—
					58.4	3.9	20.2	—	—
25i	315	ethanol	82	$C_9H_5N\text{-}O_2$	44.44	2.06	40.33	—	—
					44.6	2.2	40.6	—	—

yses (cf. Tables 1 and 2). Moreover, the mass spectra of **11c** gave m/z = 225, which corresponded to the molecular formula $C_8H_7N_3SO_3$ of the assigned structure (cf. Chart 1).

Structures **11a, 11b,** and **11c** were further investigated through their cyclization in 10% ethanolic KOH to afford 8-cyano-7-hydroxythiazolo[3,2-a]pyridin-3,5-dione (**12**) with loss of a molecule each of ethanol, water, and ammonia, respectively. Moreover, its mass spectrum gave m/z = 208, which corresponds to the molecular weight of $C_8H_4N_2SO_3$ assigned to the structure (cf. Chart 1). Compound **3** also reacted with both chloroacetone (**13a**) and 3-chloropentane-2,4-dione (**13b**) with loss of hydrogen chloride to afford the corresponding 2-S-acetonylpyridinone **14a** and 2-S-diacetylmethylpyridinone **14b,** respectively. The structures of **14a,b** were confirmed by their cyclization in 10% ethanolic KOH to afford 8-cyano-7-hydroxy-3-methylthiazolo[3,2-a]-pyridin-5-one and 2-acetyl-8-cyano-7-hydroxy-3-methylthiazolo[3,2-a]-pyridin-5-one **15a,b,** respectively. The structures of both **14a,b** and **15a,b** were also established on the bases of elemental analyses and IR and ^{1}H-NMR spectral data (cf. Tables 1 and 2). Furthermore, the mass spectra of **14a** and **15b,** as typical examples, gave m/z = 224 and 266, corresponding to the molecular formulas $C_9H_8N_2SO_3$ and $C_{11}H_{10}N_2SO_4$, respectively (cf. Chart 2).

In a similar manner, compound **3** reacted with each phenacyl bromide (**16**) and ethyl-α-chloroacetoacetate (**19**) with loss of hydrogen bromide or hydrogen chloride to afford compounds **17** and **20,** respectively. The structures of both **17** and **20** were established based on IR and ^{1}H-NMR spectroscopy and on elemental analyses data (cf. Tables 1 and 2). Furthermore, the mass spectra of **17** and **20** gave m/z = 286 and 296, corresponding to the molecular formulas $C_{14}H_{10}N_2SO_3$ and $C_{12}H_{12}N_2SO_5$, respectively, of the assigned structures (cf. Chart 2).

A further confirmation of structures **17** and **20** was obtained by their cyclization in an ethanolic solution of 10% KOH to afford the products **18** and **21,** respectively, with loss of a water molecule in each case. The structures of both **18** and **21** were confirmed based on IR and ^{1}H-NMR spectroscopy and on elemental analyses (cf. Tables 1 and 2). Moreover, the mass spectra of **18** and **21** gave m/z = 268 and 278, respectively, corresponding to the molecular formulas $C_{14}H_8N_2SO_2$ and $C_{12}H_{10}N_2SO_4$ of the assigned structures (cf. Chart 2).

The study was extended to investigate the reactivity of **3** toward hydrazine hydrate. Thus, pyrazolo[3,4-b]pyridinone **8,** prepared according to a literature procedure [13,14], reacted with nitrous acid to give the 3-diazotized pyrazolo[3,4-b]pyridinone **9,** a versatile starting material owing to the presence of more than one active site.

Compound **9** coupled with diethyl malonate to afford **24a.** The IR spectrum of this product showed the bands of OH, NH, CO ester, and CO amide groups. Its ^{1}H-NMR spectrum revealed the signals of CH_3CH_2 (triplet and quartet) protons, in addition to the signals of NH, OH, and pyridinone H-5 protons (cf. Table 2). Moreover, the mass spectrum of this product gave m/z = 337, which represented the molecular weight corresponding to a molecular formula $C_{13}H_{15}N_5SO_6$ of the assigned structure (cf. Chart 3). The previous data in addition to elemental analyses indicate **24a** to be 3-hydrazonopyrazolo[3,4-b]pyridinone (cf. Tables 1 and 2 and Chart 3).

Additional evidence in support of structure **24a** was obtained by its cyclization in an ethanolic solution containing a catalytic amount of triethylamine to afford the corresponding fused triazine

TABLE 2 IR and H-NMR Spectral Data of the Newly Synthesized Compounds

Comp.	*IR* (cm^{-1})	*^{1}H-NMR* (δ)
6a	3430, 3325 (NH_2); 3225–2500 (broad OH); 2215 (CN) and 1695 (CO amidic).	6.9–8.2 (m, 7H, ArH's, Pyridine H-5 and thiazine H-6 protons: 9.7* (s, br., 4H, two NH_2) and 12.3* (s, br., 1H, OH enolic).
6b	3421, 3317 (NH_2); 3235–2493 (broad OH); 2219 (CN) and 1687 (CO amidic).	7.0–8.1 (m, 6H, aromatic, Pyridine H-5 and thiazine H-6 protons); 9.5* (s, br., 4H, two NH_2) and 12.0* (s, br., 1H, OH enolic).
6c	3435, 3341 (NH_2); 3225–2517 (broad OH); 2220 (CN) and 1685 (CO amidic).	6.2–7.6 (m, 5H, Furyl, Pyridine H-5 and thiazine H-6 protons); 9.1* (s, br., 4H, two NH_2) and 12.2* (s, br., 1H, OH enolic).
6d	3432, 3312 (NH_2); 3218–2510 (broad OH); 2218 (CN) and 1690 (CO amidic).	6.8–8.1 (m, 7H; aromatic, Pyridine H-5 and thiazine H-6 protons: 9.4 *(s, br., 4H, two NH_2) and 12.5* (s, br., 1H, OH enolic).
6e	3445, 3332 (NH_2); 3220–2500 (broad OH); 2217 (CN) and 1700, 1685 (two CO amidic)	6.8–7.9 (m, 6H, ArH's, pyridine H-5 and thiazine H-6 protons); 9.8* (s, br., 4H, two NH_2) and 12.5* (s, br., 1H, OH enolic).
6f	3429, 3328 (NH_2); 3232–2498 (broad OH); 2222 (CN) and 1690 (CO amidic).	6.3–7.4 (m, 5H, Furyl, Pyridine H-5 and thiazine H-6 protons); 9.2 *(s, br., 4H, two NH_2) and 12.3* (s, br., 1H, OH enolic).
11a	3275 (NH); 3200–2480 (broad OH); 2213 (CN), 1715 (CO ester) and 1690 (CO amide).	1.0 (t, 3H, $CH_2\underline{CH_3}$; 2.7 (s, 2H, S-CH_2); 4.3 (q, 2H, $\underline{CH_2}CH_3$); 6.9 (s. 1H. pyridine H-5; 8.2* (s, br., 1H, NH) and 12.3* (s, br., 1H, OH enolic).
11b	3291 (NH); 3222–2485 (broad OH); 2218 (CN), 1710 (CO acid) and 1695 (CO amide).	2.8 (s, 2H, S-CH_2); 7.1 (s, 1H, pyridine H-5; 8.3* (s, br. 1H, NH) and 12.5* (s, br., 2H, 2OH enolic).
11c	3440, 3330 (NH_2); 3252 (NH); 3198–2500 (broad OH); 2220 (CN), and 1695 (CO amide).	2.7 (s, 2H, S-CH_2); 6.9 (s, 1H, pyridine H-5); 8.2* (s, br. 1H, NH); 9.4 (s, br., 2H, NH_2) and 12.5* (s, br., 1H, OH enolic).
12	3219–2508 (broad OH); 2215 (CN); and 1693 (CO amide).	4.3 (s, 2H, thiazole -Ch_2-); 6.7 (s, 1H, pyridine H-5) and 12.2* (s, br., 1H, OH).
14a	3290 (NH); 3200–2500 (broad OH); 2217 (CN); 1708 (CO acetyl) and 1695 (CO amide).	1.8 (s, 3H, $COCH_3$); 2.6 (s, 2H, S-Ch_2); 6.6 (s, 1H, pyridine H-5); 8.3* (s, br, 1H, NH) and 12.0* (s, br., 1H, OH).
14b	3315 (NH); 3224–2514 (broad OH); 2221 (CN); 1715 (CO acetyl) and 1690 (CO amide).	1.6 (s, 6H, two CO$\underline{CH_3}$); 6.2 (s, 1H, pyridine H-5); 8.4* (s, br, 1H, NH) and 12.5* (s, br., 1H, OH).
15a	3242–2350 (broad OH); 2213 (CN) and 1687 (CO amidic).	1.3 (s, 3H, CH_3); 4.8 (s, 1H, thiazole H_4-5); 6.6 (s, 1H, Pyridine H-5); and 12.3* (s, br., 1H, OH enolic).
15b	3250–2250 (broad OH); 2218 (CN); 1710 (CO acetyl) and 1690 (CO amidic).	1.1 (s, 3H, CH_3); 1.9 (s, 3H, CH_3CO); 6.8 (s, 1H, Pyridine H-5); and 12.2* (s, br., 1H, OH enolic).
17	3300 (NH) 3220–2500 (broad OH) 2215 (CN); 1704 (CO benzoyl) and 1693 (CO amidic).	2.7 (s, 2H S-CH_2); 6.9–7.8 (m, 6H, ArH's and Pyridine H-5); 8.3* (s, br., 1H, NH). And 12.3* (s, br., 1H, OH enolic).
18	3250–2500 (broad OH); 2213 (CN) and 1695 (CO amide).	4.6, (s, 1H, thiazole H-5); 6.9–8.1 (m, 6H, ArH's and Pyridine H-5) and 12.3* (s, br., 1H, OH enolic).
20	3285 (NH); 3219–2507 (broad OH); 2217 (CN); 1728 (CO esta and 1690 (amide CO)	1.0 (t, 3H, $CH_2\underline{CH_3}$); 1.9 (s, 3H, CH_3 CO); 2.9 (s, 1H, SCH); 4.3 (q, 2H, $\underline{CH_2}$-CH_3), 6.8 (s, 1H, Pyridine H-5); 3.8* (s, br., 1H NH) and 12.3* (s, br., 1H, OH enolic).
21	3217–2520 (broad OH); 2215 (CN); 1730 (CO ester) and 1695 (CO amide).	1.0 (t, 3H, $CH_2\underline{CH_3}$); 1.5 (s, 3H, CH_3); 4.2 (q, 2H, $\underline{CH_2}CH_3$); 6.8 (s, 1H, Pyridine H-5) and 12.1* (s, br., 1H, OH enolic).
24a	3315, 3300, 3285 (Three NH); 3200–2500 (broad OH); 1732 (CO ester); 1689 (CO amide and 1600 (C = C).	0.95 (t, 6H, two $\underline{CH_3}CH_2$); 4.3 (q, 4H, two $CH_3\underline{CH_2}$); 5.5* (s, br., 2H, two NH at 3-position of pyrazole residue and of pyrazole ring); 6.4 (s, 1H, pyridine H-5); 8.3* (s, br., 1H, NH on pyridine nitrogen) and 12.2* (s, br., 1H, OH).
24b	3321, 3297, 3274 (three NH); 3239–2512 (broad OH); 1741 (CO ester); 1702 (CO acetyl); 1687 (CO amide) and 1605 (C = C).	1.1 (t, 3H, $\underline{CH_3}CH_2$); 2.3 (s, 3H, $CO\underline{CH_3}$); 4.2 (q, 2H, $CH_3\underline{CH_2}$); 5.6* (s, br., 2H, two NH at 3-position of pyrazole residue and that of pyrazole ring); 6.6 (s, 1H, pyridine H-5); 8.2* (s, br., 1H, NH on pyridine nitrogen) and 12.5* (s, br., 1H, OH).

TABLE 2 (*Continued*)

Comp.	*IR* (cm^{-1})	*^{1}H-NMR* (δ)
24c	3336, 3314, 3278 (three NH); 3239–2512 (broad OH); 1710 (CO ester); 1695 (CO amide) and 1602 (C = C).	1.7 (t, 6H, two $CO\underline{CO_3}$); 5.1* (s, br., 2H, two NH at 3-position of pyrazole residue and that of pyrazole ring); 6.3 (s, 1H, pyridine H-5); 8.2* (s, br., 1H, NH on pyridine nitrogen) and 12.0* (s, br., 1H, OH).
24d	3450, 3412, 3300, 3290 (NH_2 and NH); 3200–2500 (broad OH); 2214 (CN); 1687 (CO amide) and 1550 (C = S)	5.3* (s, br., 2H, two NH, of pyrazole ring and at 3-position of this ring); 6.2* (s, br., 2H, $\underline{NH_2}$); 6.5 (s, 1H, pyridine H-5); 8.1* (s, br., 1H, NH on pyridine nitrogen) and 12.3* (s, br., 1H, OH)
24e	3423, 3400, 3313, 3276 (NH_2 and NH); 3200–2519 (broad OH); 2222 (CN) and 1692 (CO amide).	5.2* (s, br., 2H, two NH, of pyrazole ring and that of 3-position of this ring); 6.0* (s, br., 2H, $\underline{NH_2}$); 6.5 (s, 1H, pyridine H-5); 8.3* (s, br., 1H, NH on pyridine nitrogen) and 12.5* (s, br., 1H, OH)
24f	3270, 3220, 3197 (three NH); 3200–2500 (broad OH); 2219 (CN); 1708 (CO ketone), 1687 (CO amide) and 1602 (C = C)	5.5* (s, br., 2H, two NH of pyrazole and its 3-position); 6.3 (s, 1H, pyridine H-5), 7.5–8.3 (m, 6H, ArH's and $N\underline{H}$ of the pyridine residue) and 12.5* (s, br., 1H, OH).
24g	3290, 3245, 3212 (three NH); 3208–2520 (broad OH); 2222 (CN); 1728 (CO ester), 1692 (CO amide) and 1604 (C = C).	1.1 (t, 3H, $\underline{CH_3}CH_2$); 4.2 (q, 2H, CH_3-$\underline{CH_2}$); 5.3* (s, br., 2H, two NH at 3-position of pyrazole and its NH); 6.5 (s, 1H, pyridine H-5), 8.2* (s, br., 1H, $N\underline{H}$ of pyridine and 12.2* (s, br., 1H, OH).
24h	3293, 3237, 3210 (three NH); 3200–2522 (broad OH); 1732 (CO ester); 1710 (CO ketone); 1693 (CO amide) and 1600 (C = C).	1.2 (t, 3H, $\underline{CH_3}CH_2$); 4.2 (q, 2H, $CH_3\underline{CH_2}$); 5.5* (s, br., 2H, two NH at 3-position of the pyrazole residue and its NH), 6.3 (s, 1H, pyridine H-5); 7.5–8.3 (m, 6H, ArH's and NH of pyridine.)
25a	3300, 3235 (two NH); 3200–2542 (broad OH); 1719 (CO ester); 1692 (CO amide) and 1600 (C = C).	1.0 (t, 3H, $\underline{CH_3}CH_2$); 4.1 (q, 2H, CH_3-$\underline{CH_2}$); 6.2 (s, 1H, pyridine H-5); 8.3* (s, br., 2H, two NH of pyridine and triazine) and 12.0* (s, br., 1H, OH).
25b	3300 (NH); 3200–2513 (broad OH); 1723 (CO ester); 1695 (CO amide) and 1600 (C = C).	0.96 (t, 3H, $\underline{CH_3}CH_2$); 1.5 (s, 3H, CH_3); 4.3 (q, 2H, $CH_3\underline{CH_2}$); 6.4 (s, 1H, pyridine H-5); 8.1* (s, br., 2H, two NH of pyridine and triazine) and 12.3* (s, br., 1H, OH).
25c	3287 (NH); 3200–2500 (broad OH); 1708 (CO acetyl); 1689 (CO amide) and 1601 (C = C).	1.2 (s, 3H, CH_3); 2.3 (s, 3H, $CO\underline{CH_3}$); 6.2 (s, 1H, pyridine H-5); 8.2* (s, br., 2H, two NH of pyridine and triazine) and 12.5* (s, br., 1H, OH).
25d	3452, 3423, 3397, 3278 (NH_2 and NH); 3209–2532 (broad OH); 1689 (CO amide), 1601 (C = C) and 1553 (C = S).	4.9 (s, br., 2H, NH_2 at 5-position of triazine ring); 5.7* (s, br., 2H, $\underline{NH_2}$ of $CSNH_2$); 6.3 (s, 1H, pyridine H-5); 8.1* (s, br., 1H, NH, of pyridine) and 12.3* (s, br., 1H, OH).
25e	3421, 3397, 3273 (NH and NH_2); 3215–2530 (broad OH); 1687 (CO amide) and 1604 (C = C).	4.7* (s, br., 2H, NH_2 at 5-position of triazine ring); 5.9* (s, br., 2H, $\underline{NH_2}$ of $CONH_2$); 6.4 (s, 1H, pyridine H-5); 8.3* (s, br., 1H, NH, of pyridine) and 12.5* (s, br., 1H, OH).
25f	3438, 3383, 3268 (NH_2 and NH); 3229–2509 (broad OH); 1719 (CO ketone); 1683 (CO amide) and 1602 (C = C).	5.3* (s, br., 2H, NH_2 at 5-position of triazine ring); 6.2 (s, 1H, pyridine H-5) 7.5–8.1 (m, 6H, ArH's and pyridine NH) and 12.5* (s, br., 1H, OH)
25g	3441, 3398, 3276 (NH_2 and NH); 3228–2539 (broad OH); 1732 (CO ester); 1689 (CO amide) and 1605 (C = C).	0.95 (t, 3H, $\underline{CH_3}CH_2$); 4.2 (q, 2H, $CH_3\underline{CH_2}$); 4.9* (s, br., 2H, NH_2 at 5-position of triazine ring); 6.3 (s, 1H, pyridine H-5); 8.1* (s, br., 1H, NH of pyridine ring) and 12.5* (s, br., 1H, OH).
25h	3276 (NH); 3217–2528 (broad OH); 1732 (CO ester); 1690 (CO amide) and 1604 (C = C).	1.0 (t, 3H, $\underline{CH_3}CH_2$); 4.1 (q, 2H, CH_3-$\underline{CH_2}$); 6.0 (s, 1H, pyridine H-5); 7.4–8.3 (m, 6H, ArH's and NH of pyridine ring) and 12.3* (s, br., 1H, OH).
25i	3432, 3392, 3227 (NH_2 and NH); 3200–2532 (broad OH); 2218 (CN); 1694 (CO amide) and 1600 (C = C).	4.8* (s, br., 2H, NH_2 at 5-position of triazine ring); 6.2 (s, 1H, pyridine H-5); 8.4* (s, br., 1H, NH of pyridine ring) and 12.3* (s, br., 1H, OH).

Signals of all asterisked protons were lost on D_2O addition.

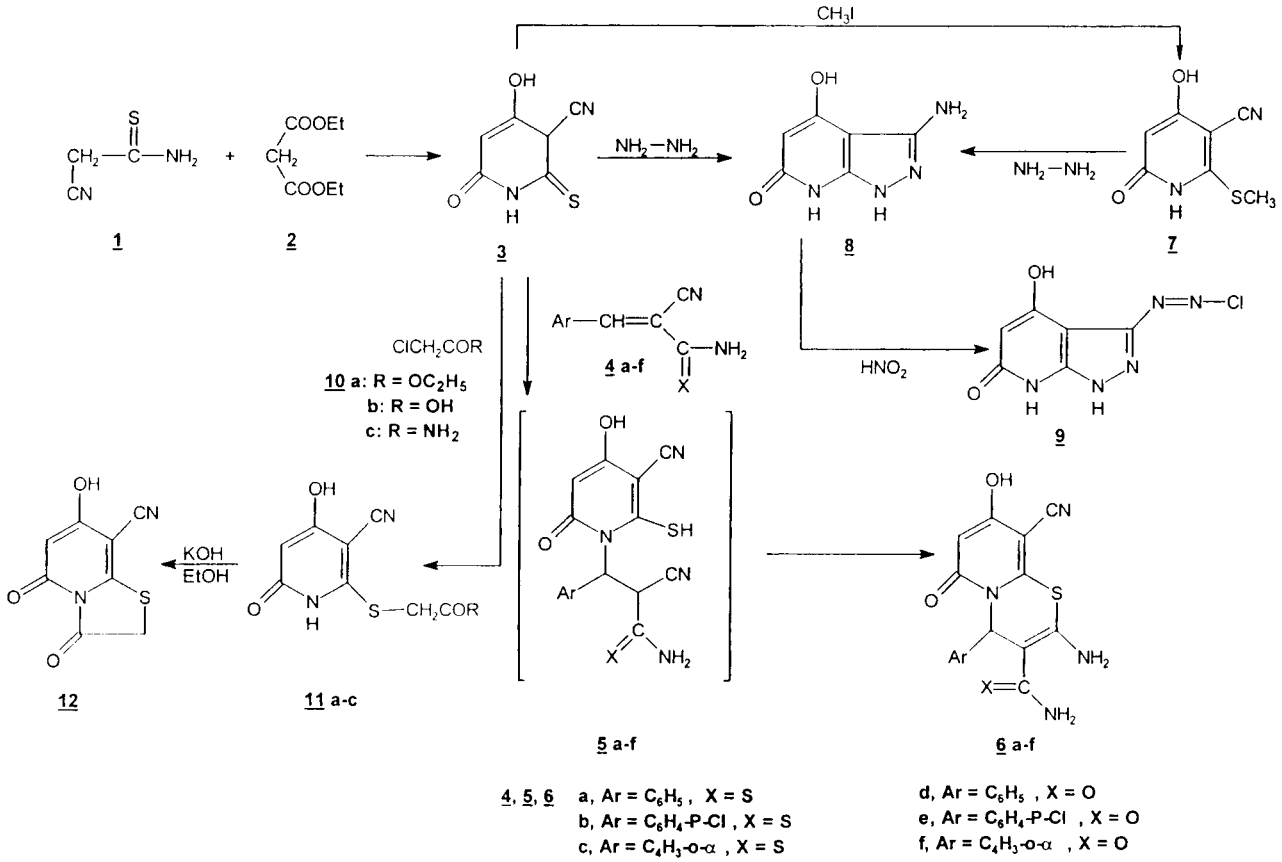


CHART 1

25a. The structure of **25a** was established based on IR and ^{1}H-NMR spectroscopy and also on elemental analyses (cf. Tables 1 and 2). Its mass spectrum gave m/z = 291, corresponding to molecular formula $C_{11}H_9N_5O_5$ of the assigned structure (cf. Chart 3). The detected m/z = 291 of **25a** indicates that the ring closure of **24a** (m/z = 337) involves liberation of ethanol (molecular weight = 46) (cf. Chart 3). Additional evidence for structure **25a** is provided by its synthesis via another route. Thus, the diazonium chloride **9** reacted with diethyl malonate (**23a**) in refluxing ethanol containing a catalytic amount of triethylamine to give **25a** (cf. Chart 3).

In a similar way, the diazonium salt **9** was coupled with ethyl acetoacetate (**23b**), pentane-2,4-dione (**23c**), α-cyanothioacetamide (**23d**), α-cyanoacetamide (**23e**), ω-cyanoacetophenone (**23f**), ethyl cyanoacetate (**23g**), and ethyl benzoylacetate (**23h**) in cold ethanol containing sodium acetate to afford a product with loss of hydrogen chloride in each case. The IR spectra of these reaction products showed the bands of OH, NH, and CO amide groups in addition to other bands of the CO group in the cases of **23b–h** and bands CN and NH_2 groups in the cases of **23d–g.** The ^{1}H-NMR spectra in the cases of **23b,g,h** revealed the quartet and triplet signals of ethyl protons in addition to the signals of pyridine H-5, NH, and OH protons. The ^{1}H-NMR spectra of **23d,e** revealed the signals of NH_2 protons in addition to pyridine H-5, NH, and OH protons. The ^{1}H-NMR spectrum of **23f** revealed the signals of aromatic protons, whereas, in the case of **23c,** the signal of CH_3 protons was detected in addition to the signals of pyridine H-5, NH, and OH protons in each case. Considering the elemental analyses and the above-mentioned spectral data (cf. Tables 1 and 2), these reaction products were formulated as the corresponding hydrazones of 3-diazotized pyrazolo[3,4-b]pyridinones **24b–h.** Moreover, the mass spectra of **24c,e,h** as typical examples of the series gave m/z = 277, 261, and 369, respectively, consistant with the molecular formulas $C_{11}H_{11}N_5O_4$, $C_9H_7N_7O_3$, and $C_{17}H_{15}N_5O_5$, respectively, of the assigned structures (cf. Chart 3).

Compounds **24b–h** were cyclized in refluxing ethanol containing a catalytic amount of triethyl-

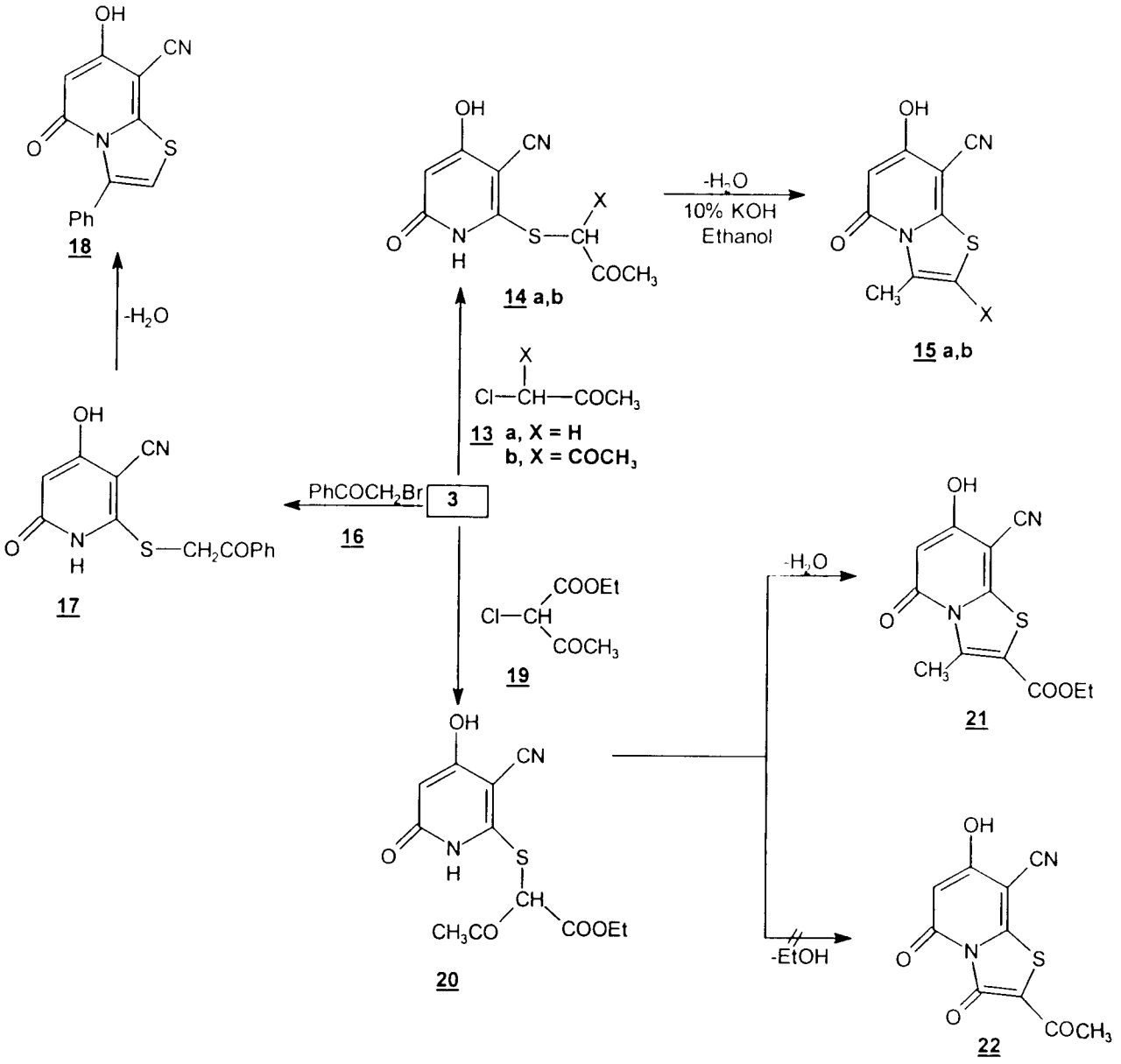
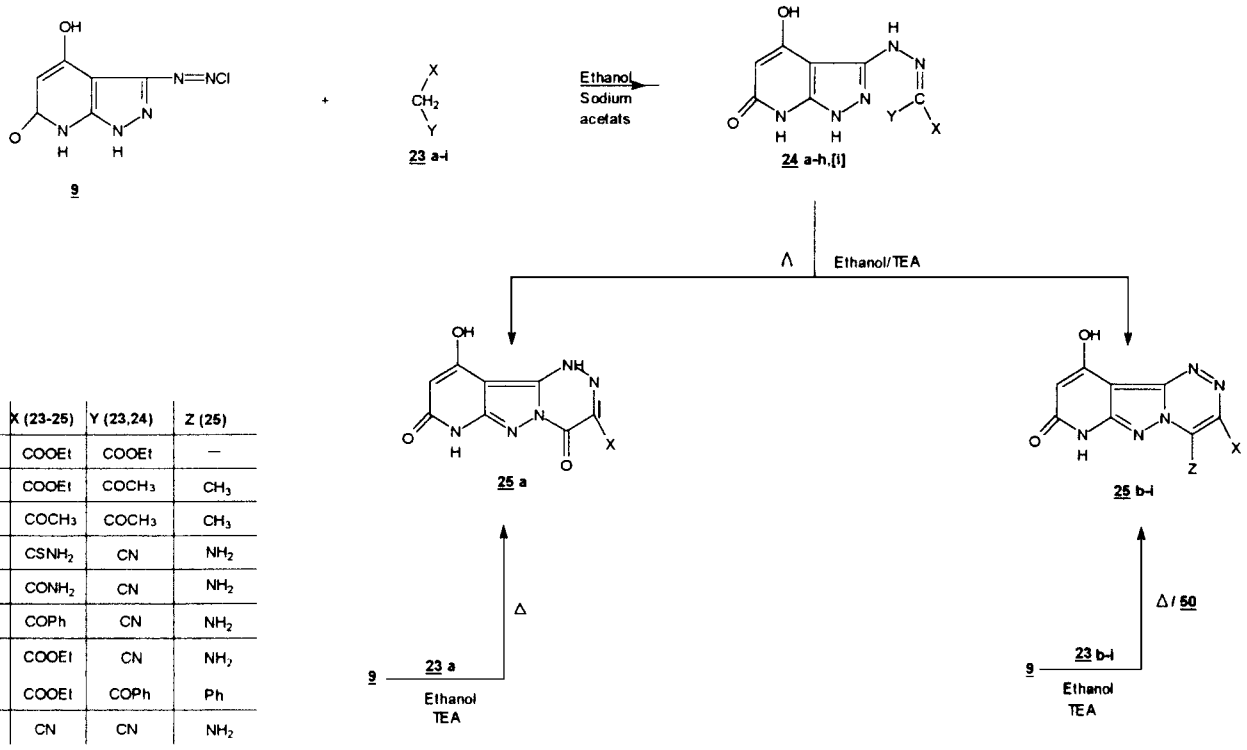


CHART 2

amine to afford the corresponding pyrido[2,3: 4′,5′]pyrazolo[5,1-a]-1,2,4-triazines **25b–h** via an addition to the CN group in the cases of **24d–g** and liberation of a water molecule in the cases of **24b,c,h.** The structures of **25b–h** were established based on elemental analyses and on IR and ^{1}H-NMR spectral data (cf. Tables 1 and 2). Moreover, the mass spectra of **25c,e,h** as typical examples gave *m/z* = 259, 261, and 351, corresponding to the molecular formulas $C_{11}H_9N_5O_3$, $C_9H_7N_7O_3$, and $C_{17}H_{13}N_5O_4$, respectively (cf. Chart 3). A further confirmation of structures **25b–h** was given through their syntheses via another route; thus, diazonium salt (**9**) was coupled with **23b–h** in refluxing ethanol containing a catalytic amount of triethylamine to afford directly **25b–h** (cf. Tables 1 and 2 and Chart 3).

In contrast to the behavior of **23a–h** through coupling with 3-diazotized aminopyrazolo[3,4-b]pyridinone **9,** malanonitrile **23i** coupled with the diazonium salt **9** under the above-mentioned conditions to afford directly **25i** whose structure was established based on IR and ^{1}H-NMR spectra and on elemental analyses (cf. Tables 1 and 2). All attempts to isolate the corresponding hydrazone (**24i**) failed under a variety of conditions. Additional support for structures **25b–i** was given by UV spectrophotometry



	X (23-25)	Y (23,24)	Z (25)
a	COOEt	COOEt	–
b	COOEt	$COCH_3$	CH_3
c	$COCH_3$	$COCH_3$	CH_3
d	$CSNH_2$	CN	NH_2
e	$CONH_2$	CN	NH_2
f	COPh	CN	NH_2
g	COOEt	CN	NH_2
h	COOEt	COPh	Ph
i	CN	CN	NH_2

CHART 3

that showed peaks at ≅332 ± 5 nm, which is attributable to the presence of the −N=N− moiety.

EXPERIMENTAL

All melting points are uncorrected. The IR spectra in KBr discs were recorded on Perkin-Elmer FT-IR type 4 and Pye Unicam SP-1100 spectrophotometers. The ^{1}H-NMR spectra were recorded on Varian EM 390-90 MHz, Gemini 200, Varian NMR spectrometer (200 MHz), and Brucker WP-80 spectrometers using $CDCl_3$, DMSO-d_6, and $(CD_3)_2CO$ as solvents and TMS as an internal standard. Chemical shifts are expressed as δ units. Mass spectra were recorded on a Hewlett-Packard GC-MS type 2988 series A using the DIP technique at 70 eV. Microanalyses were performed at the Microanalytical Center of Cairo University using a Perkin-Elmer 2400 CHN Elemental Analyzer.

Compounds **3**, **7**, and **8** were prepared according to a literature procedure [13,14].

Syntheses of **6a–f.** A solution of **3** (0.01 mole) in ethyl alcohol (50 mL) containing a catalytic amount of triethylamine (0.5 mL) was heated under reflux for 5 hours with each of the cinnamonitriles **4a–f**. The solid products isolated from the hot mixture, or after cooling, were filtered off and crystallized from the proper solvent to afford **6a–f**, respectively (cf. Tables 1 and 2).

Syntheses of **9.** A cold solution of **8** (0.01 mole) in concentrated hydrochloric acid (1 mL) was treated with a cold saturated solution of sodium nitrite (0.015 mole), and the mixture was then stirred in an ice bath for 1–2 hours. The solid product obtained was filtered off, washed with water, and crystallized from ethanol to afford **9** (cf. Tables 1 and 2).

Syntheses of **11a–c**, **14a,b**, **17**, *and* **20***: General Procedure.* A solution of **3** (0.01 mole) in methanolic sodium methoxide solution (0.01 gram atom of sodium metal added to 100 mL methanol) was treated with 0.01 mole each of ethyl chloroacetate (**10a**), chloroacetic acid (**10b**), chloroacetamide (**10c**), chloroacetone (**13a**), 3-chloro-2,4-pentanedione (**13b**), ω-bromoacetophenone (**16**), and ethyl α-chloroacetoacetate (**19**). Each reaction mixture was heated under reflux for 5 hours, then cooled, poured into ice-cooled water, and then acidified with concentrated hydrochloric acid. The solid products obtained were filtered off, washed with water, and crystallized from the proper solvent to afford **11a–c**, **14a,b**, **17**, and **20**, respectively (cf. Tables 1 and 2).

Syntheses of **12**, **15a–d**, **18**, *and* **21***: General Procedure.* A solution of each **11a–c**, **14a,b**, **17**, and **20**

(0.01 mole each) in ethanol (50 mL) was heated under reflux for 5 hours with KOH (≅0.02 mole). The reaction mixture was cooled and acidified with concentrated hydrochloric acid, and the solids obtained were filtered off and washed with water. The isolated solids were crystallized from the proper solvent to yield **12**, **15a–d**, **18**, and **21**, respectively (cf. Tables 1 and 2).

Syntheses of **24a–h***: General Procedure.* A solution of **9** (0.01 mole) in the presence of sodium acetate (1 g) was treated with each of **23a–h** (0.01 mole), and the whole was stirred in an ice bath for 1–2 hours. The solids obtained were filtered off, washed with water, and crystallized from the proper solvent to yield **24a–h** (cf. Tables 1 and 2).

Syntheses of **25a–h**

Route A. A solution of each **24a–h** in ethanol containing a catalytic amount of triethylamine (0.5 mL) was heated under reflux for 3–5 hours. The solid products obtained were filtered off and crystallized from the proper solvent to afford **25a–h** (cf. Tables 1 and 2).

Route B. A solution of **9** (0.01 mole) in ethanol containing a catalytic amount of triethylamine (0.5 mL) was treated with each of **23a–i** (0.01 mole) under reflux for 5 hours. The solid products obtained from the hot mixture, or after cooling, were filtered off and crystallized from the proper solvent to yield **25a–i** (cf. Tables 1 and 2).

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