SYNTHESIS AND SOME REACTIONS OF THIENO[2,3-*d*]PYRIMIDINES AND S-SUBSTITUTED MERCAPTOPYRIDINES

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Ethyl 3-cyano-4,6-diphenyl-2-pyridylthioacetate (*II*) yielded with hydrazine hydrate hydrazides *III*, *IV* that both proved to be versatile compounds for the synthesis of new heterocyclic derivatives. Thus the thieno[2,3-*b*]pyridine derivatives *Xa* – *Xd* and the thiazolidinone[1] derivatives *XIa* – *XId* and *XIIa* – *XIId* were obtained.

EXPERIMENTAL

All melting points are uncorrected. The IR spectra (KBr, given in cm^{-1}) were run on a Pye–Unicam apparatus SP3-100 and the ^1H NMR spectra (in ppm, δ-scale) were recorded on Varian EM-390 (90 MHz) spectrometer using TMS as internal standard.

Ethyl (3-Cyano-4,6-diphenyl-2-pyridylthio)acetate (*II*)

A mixture of *I* (14.4 g, 0.05 mol), fused sodium acetate (6.15 g, 0.07 mol) in ethanol (100 ml) and ethyl chloroacetate (6.7 g, 0.055 mol) was heated under reflux for 4 h. On cooling, the precipitate was collected and recrystallized from dioxane as yellow crystalls of *II*. IR spectrum: 2 200 (CN), 1 740 (CO); ^1H NMR spectrum ($CDCl_3$): 3.90 s, 2 H (SCH_2); 4.17 q, 2 H (CO_2CH_2), 1.30 t, 3 H (CH_3), 7.10 – 7.60 m, 11 H (arom.).

(3-Cyano-4,6-diphenyl-2-pyridylthio)acetylhydrazine (*III*) and 3-Amino-4,6-diphenylthieno[2,3-*b*]pyridine-2-carbohydrazide (*IV*)

A mixture of *II* (5 g, 0.0134 mol) and hydrazine hydrate (99%, 20 ml) in absolute ethanol (50 ml) was heated under reflux for 3 h. The reaction mixture was cooled, filtered off and the precipitate was recrystallized from dioxane to give yellow crystalls of *III*. IR spectrum: 2 210 (CN), 1 680 (CO). The mother liquor was diluted with water, and the precipitated solid was collected and recrystallized from ethanol to give *IV*. IR spectrum: 3 350, 3 250 ($NHNH_2$); 3 400, 3 450 (NH_2), 1 590 (CN), 1 670 (CO).

1-(3-Cyano-4,6-diphenyl-2-pyridylthio)acetyl-4-phenylsemicarbazide (*V*)

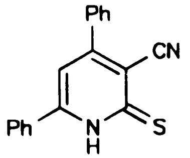
A mixture of *III* (1 g, 0.0028 mol) and phenylisocyanate (0.3 ml, 0.0025 mol) in absolute ethanol (20 ml) was heated under reflux for 5 h. The buff precipitated product obtained on cooling was recrystallized from dioxane. IR spectrum: 3 350, 3 290 (NH), 2 210 (CN), 1 720 (CO).

1-(3-Cyano-4,6-diphenylthio)acetyl-4-phenylthiosemicarbazide (*VI*)

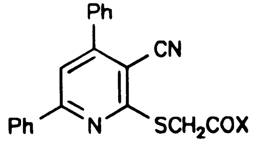
A mixture of *III* (1 g, 0.0028 mol) and phenylisothiocyanate (0.4 ml, 0.003 mol) in absolute ethanol (20 ml) was heated under reflux for 5 h. The yellow crystalline product obtained on cooling was recrystallized from dioxane. IR spectrum: 3 350, 3 300 (NH), 2 210 (CN), 1 200 (CS), 1 720 (CO).

3-Cyano-4,6-diphenyl-2-(3,5-dimethyl-1-pyrazolylcarbonylmethylthio)pyridine (*VII*)

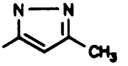
A mixture of *III* (1 g, 0.0028 mol) and acetylacetone (0.3 ml, 0.0092 mol) in ethanol (20 ml) was heated under reflux for 6 h. The precipitated solid was collected and recrystallized from dioxane. IR spectrum: 2 220 (CN) and 1 680 (CO).



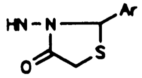
I

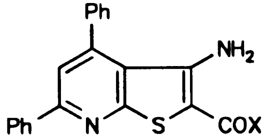


II, X = OEt
III, X = $NHNH_2$
V, X = NHNHCONHPh
VI, X = NHNHCSNHPh
VII, X =

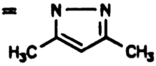


IX, X = NHN=CHAr
XI, X =

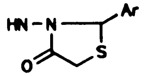




IV, X = $NHNH_2$
VIII, X =

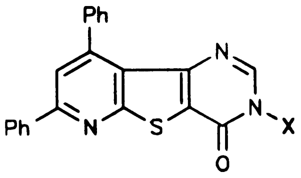


X, X = NHN=CHAr
XII, X =

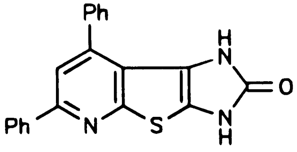


XV, X = N_3

In formulae *IX* – *XII* : *a*, Ar = C_6H_5; *b*, Ar = *p*-$CH_3OC_6H_4$;
c, Ar = *p*-ClC_6H_4; *d*, Ar = *p*-$NO_2C_6H_4$



XIII, X = NHCHO
XIV, X = $N(Ac)_2$



XVI

TABLE I
Physical and analytical data for compounds (*I* – *XVI*)

Compound	M. p., °C Yield, %	Formula (M. w.)	Calculated/Found			
			% C	% H	% N	% S
I	252 – 254	$C_{18}H_{12}N_2S$	74.97	4.19	9.71	11.12
	90	(288.4)	74.88	4.13	9.63	11.20
II	167 – 169	$C_{22}H_{18}N_2O_2S$	70.57	4.85	7.48	8.56
	80	(374.5)	70.68	4.94	7.55	8.61
III	254 – 267	$C_{20}H_{16}N_4OS$	66.65	4.47	15.54	8.90
	50	(360.4)	66.71	4.55	14.48	8.82
IV	314 – 316	$C_{20}H_{16}N_4OS$	66.65	4.47	15.54	8.90
	50	(360.4)	66.55	4.51	15.61	8.83
V	319 – 321	$C_{27}H_{21}N_5O_2S$	67.62	4.41	14.60	6.69
	65	(479.6)	67.72	4.47	14.54	6.73
VI	194 – 196	$C_{27}H_{21}N_5OS_2$	65.43	4.27	14.13	12.94
	72	(495.6)	65.51	4.32	14.06	12.86
VII	309 – 311	$C_{25}H_{20}N_4OS$	70.73	4.75	13.20	7.55
	55	(424.5)	70.64	4.71	13.15	7.61
VIII	191 – 193	$C_{25}H_{20}N_4OS$	70.73	4.75	13.20	7.55
	68	(424.5)	70.65	4.66	13.13	7.46
IXa	311 – 313	$C_{27}H_{20}N_4OS$	72.30	4.49	12.49	7.15
	60	(448.6)	72.41	4.54	12.42	7.24
IXb	309 – 311	$C_{28}H_{22}N_4O_2S$	70.27	4.63	11.71	6.70
	65	(478.6)	70.36	4.57	11.80	6.65
Xa	292 – 294	$C_{27}H_{20}N_4OS$	72.30	4.49	12.49	7.15
	80	(448.6)	72.42	4.52	12.54	7.21
Xb	211 – 213	$C_{28}H_{22}N_4O_2S$	70.27	4.63	11.71	6.70
	80	(478.6)	70.36	4.58	11.65	6.62
Xc[a]	284 – 286	$C_{27}H_{19}ClN_4OS$	67.14	3.97	11.60	6.64
	87	(483.0)	67.22	3.91	11.52	6.59
Xd	296 – 298	$C_{27}H_{19}N_5O_3S$	65.71	3.88	14.19	6.50
	90	(493.6)	65.65	3.92	14.25	6.41
XIa	>340	$C_{29}H_{22}N_4O_2S_2$	66.65	4.24	10.72	12.27
	52	(522.7)	66.71	4.29	10.81	12.34
XIb	>340	$C_{30}H_{24}N_4O_3S_2$	65.20	4.38	10.14	11.60
	56	(552.7)	65.11	4.43	10.06	11.54

TABLE I
(*Continued*)

Compound	M. p., °C Yield, %	Formula (M. w.)	Calculated/Found			
			% C	% H	% N	% S
XIIa	171 – 173	$C_{29}H_{22}N_4O_2S_2$	66.65	4.24	10.72	12.27
	54	(522.7)	66.72	4.30	10.66	12.32
XIIb	221 – 223	$C_{30}H_{24}N_4O_3S_2$	65.20	4.38	10.14	11.60
	60	(552.7)	65.14	4.41	10.20	11.52
XIIc	207 – 209	$C_{29}H_{21}ClN_4O_2S_2$	62.52	3.80	10.06	11.51
	58	(557.1)	62.63	3.74	10.04	11.45
XIId	279 – 281	$C_{29}H_{21}N_5O_4S_2$	61.36	3.73	12.34	11.30
	62	(567.7)	61.44	3.80	12.29	11.24
XIII	327 – 329	$C_{22}H_{14}N_4O_2S$	66.32	3.51	14.06	8.05
	86	(398.4)	66.58	3.62	14.02	8.15
XIV	247 – 249	$C_{25}H_{18}N_4O_3S$	66.07	3.99	12.33	7.05
	69	(454.5)	65.86	3.93	12.34	6.94
XV	181 – 183	$C_{20}H_{13}N_5OS$	64.68	3.53	18.86	8.63
	80	(371.4)	64.76	3.48	18.91	8.56
XVI	249 – 251	$C_{20}H_{13}N_3OS$	69.95	3.82	12.24	9.34
	60	(343.4)	70.01	3.78	12.32	9.41

[a] Calculated: 7.34% Cl; found: 7.41% Cl.

3-Amino-4,6-diphenyl-2-(3,5-dimethylpyrazol-1-yl-carbonyl)thieno[2,3-*d*]pyridine (*VIII*)

A mixture of *IV* (1 g, 0.0028 mol) and acetylacetone (0.3 ml, 0.0092 mol) was heated under reflux for 5 h. The solid formed was recrystallized from dioxane. The m.p. and spectral data are identical to that of the same compound obtained by the interaction of *VII* with alcoholic sodium ethoxide. IR spectrum: 1 680 (CO), 1 580 (CN). ^{1}H NMR spectrum ($CDCl_3$): 5.70 s, 1 H (CH-pyrazole), 4.80 s, 3 H (CH_3).

N-Benzylidene-(3-cyano-4,6-diphenyl-2-pyridylthio)acethydrazides (*IXa* – *IXb*)

A mixture of *III* (1 g, 0.0028 mol) and appropriate aromatic aldehydes (0.0028 mol) was fused together for 15 min, then heated under reflux in ethanol (20 ml) for 5 h. The product was separated and recrystallized from ethanol. IR spectra: 3 250 (NH), 2 200 (CN), 1 680 (CO) and 1 580 (CN).

^1H NMR spectra ($CDCl_3$): 7.20 – 7.80 m, 16 H (arom.); 8.20 s, 1 H (NCH); 11.10 s, 1 H (CONH) for *IXa*.

3-Amino-N-benzylidene-4,6-diphenylthieno[2,3-*b*]pyridine-2-carbohydrazides (*Xa* – *Xd*)

Method A: A mixture of *IV* (1 g, 0.0028 mol) and aromatic aldehydes (0.0028 mol) was fused together for 15 min, then heated under reflux in ethanol (50 ml) for 6 h. The product was separated out and recrystallized from ethanol.

Method B: Compounds *Xa* and *Xb* were obtained unequivocally by boiling of *IXa* and *IXb* respectively in alcoholic sodium ethoxide. IR spectra: 1 580 (CN), 3 500, 3 350 (NH_2), 3 150 (NH) and 1 690 (CO).

3-Cyano-2-[(2-aryl-3-aminocarbonylmethyl-4-thiazolidinonyl)thio]-4,6-diphenylpyridine (*XIa* – *XIb*)

A mixture of *IXa* – *IXb* (0.01 mol) and thioglycolic acid (0.01 mol) in benzene (30 ml) was heated under reflux for 20 h. The solvent was removed under reduced pressure. The residue was treated with sodium carbonate solution, filtered off and crystallized from ethanol to give the title compounds. IR spectra: 3 250 (NH), 2 200 (CN), 1 700 (CO, thiazolidinone), 1 680 (CO, amide). ^1H NMR spectra ($CDCl_3$): 7.00 – 7.70 m, 16 H (arom.); 3.8 s, 2 H (CH_2, thiazolidinone), 5.80 s, 1 H (CH, thiazolidinone); 9.80 s, 1 H (CONH).

3-Amino-4,6-diphenyl-2-(2-aryl-4-thiazolidinon-3-yl-carbonyl)thieno[2,3-*d*]pyridine (*XIIa* – *XIId*)

These compounds were obtained by the reaction of *Xa* – *Xd* with thioglycolic acid as mentioned above. The physical and analytical data are given in Table I.

3-Formylamino-7,9-diphenylpyrido[3′,2′:4,5]thieno[3,2-*d*]pyrimidin-4(3*H*)-one (*XIII*)

A suspension of *IV* (1 g, 0.0028 mol) in formic acid (20 ml) was heated under reflux for 4 h. The buff solid separated on cooling was collected and recrystallized from dioxane as yellow crystals. IR spectrum: 1 690 (CO, pyrimidine), 3 300 (NH) and 1 730 (CO, CHO). ^1H NMR spectrum ($CDCl_3$): 7.80 s, 1 H (CH, formyl group); 8.50 s, 1 H (CH, pyrimidine) and 7.20 – 7.70 m, 11 H (arom.).

3-Diacetyl-2-methyl-7,9-diphenyl[3′,2′:4,5]thieno[3,2-*d*]pyrimidine-4(3*H*)-one (*XIV*)

A mixture of *IV* (1 g, 0.0028 mol) and acetic anhydride (20 ml) was heated under reflux for 5 h. The solid product was collected and recrystallized from dioxane. IR spectrum: 1 750 (CO, $COCH_3$), 1 680 (CO; pyrimidine). ^1H NMR spectrum ($CDCl_3$): 2.70 s, 6 H (2 $COCH_3$); 2.20 s, 3 H (CH_3) and 7.00 – 7.55 m, 11 H (arom.).

3-Amino-4,6-diphenylthieno[2,3-*b*]pyridine-2-carboxylic Acid Azide (*XV*)

Sodium nitrite solution (0.01 mol, 10 ml H_2O) was added to a solution of *IV* (1 g, 0.0028 mol) in acetic acid (10 ml) at room temperature during 5 min with stirring. The stirring was continued for 2 h further. The solid product was filtered and recrystallized from ethanol. IR spectrum: 3 500 (NH_2), 2 120 (CON_3) and 1 670 (CO).

4,6-Diphenyl-1*H*-imidazolo[4',5':4,5]thieno[2,3-*b*]pyridine-2(3*H*)-one (*XVI*)

3-Amino-4,6-diphenylthieno[2,3-*b*]pyridine-2-carboxylic acid azide (0.5 g, 0.0013 mol) was heated under reflux for 30 min in xylene (20 ml). The crude product was crystallized from dilute dioxane. IR spectrum: 3 150 (NH), 1 680 (CO).

REFERENCES

1. El-Shafei A. K., Hassan Kh. M., El-Kashef H. S.: J. Indian Chem. Soc. *54*, 60 (1977).