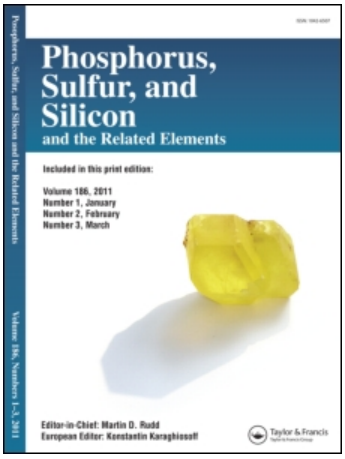

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HALOGENATION OF 3-HYDROXY-1H-PYRIDO[2,1-*B*]BENZOTHIAZOL-1-ONE: SYNTHESIS OF TWO NEW RING SYSTEMS

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COMMUNICATION
HALOGENATION OF 3-HYDROXY-1H-PYRIDO[2,1-*b*]BENZOTHIAZOL-1-ONE: SYNTHESIS OF TWO NEW RING SYSTEMS

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3-Hydroxy-1H-pyrido[2,1-b]benzothiazol-1-one (1) reacts with sulphuryl chloride to give the 2-chloro derivative **II**. Bromination of **I** yields the 4-bromo derivative **VIII**. Each of **II** and **VIII** condenses with thiourea to afford 2-amino-11H-thiazolo[4',5':4,5]pyrido[2,1-b]benzothiazol-11-one (**IV**) and 2-amino-5H-thiazolo[4',5': 4,3]pyrido[2,1-b]benzothiazol-5-one (**V**), respectively. The structures of the newly synthesised compounds are proved by chemical and spectral methods.

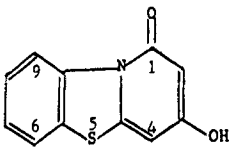
Key words: Pyridobenzothiazole; chlorination; bromination; coupling.

INTRODUCTION

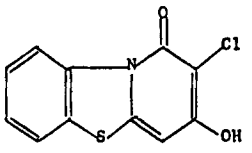
In continuation of our interest in the synthesis of polynuclear heterocyclic compounds,[1–4] we here report the halogenation of 3-hydroxy-1H-pyrido[2,1-b]benzothiazol-1-one (**I**)[5] and the use of the monohalogenated derivatives in the synthesis of heterocyclic compounds with new ring systems.

DISCUSSIONS

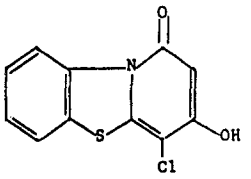
Dropwise addition of an equimolecular amount of sulphuryl chloride to a cold suspension of **I** in chloroform, yields the 2-chloro-3-hydroxy-1H-pyrido[2,1-b]benzothiazol-1-one (**II**) or the 4-chloro derivative (**III**).



I



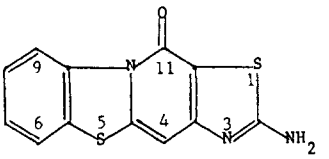
II



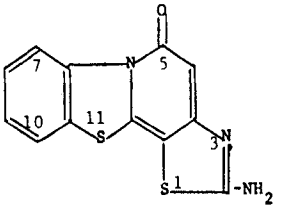
III

The ^{1}H-NMR spectrum (DMSO-d_6) of **II** shows peaks at δ 6.5 (s, 1H, disappears after D_2O exchange, OH), 7.52 (m, 3H, aromatic H-7 & H-8 + ethylenic H-4), 7.95 (d, 1H, aromatic H-9), 9.0 (d, 1H, aromatic H-6) and its ir spectrum displays absorption bands at 3150 (OH), 2800 (CH) and 1660 cm^{-1} (CO). Compound **II** reacts with thiourea in refluxing dioxane to give 2-amino-11H-thiazolo[4',5': 4,5]pyrido[2,1-b]benzothiazol-11-one (**IV**), with a new ring system.

The angular isomer **V** would result from the reaction of **III** with thiourea.



IV



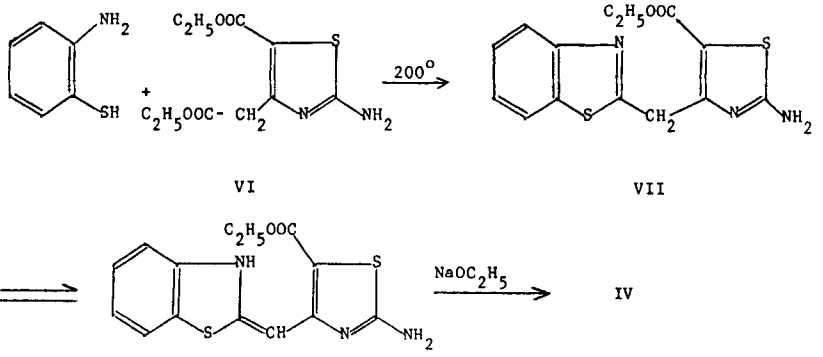
V

The ^{1}H-nmr spectrum (DMSO-d_6) of **IV** shows peaks at δ 7.15 (s, 1H, H-4), δ 7.50 (m, 2H, aromatic H-7 & H-8), 7.93 (d, 1H, aromatic H-9), 8.15 (d, 1H, aromatic H-6), 9.15 (broad s, 2H, disappears after D_2O exchange, NH_2). The assignment of structure **IV** (and hence the structure of its precursors), and not **V**, to the reaction product is based on the identity of **IV** with an authentic sample prepared by an alternative route as follows.

When 2-amino-5-ethoxycarbonyl-4-ethoxycarbonylmethylthiazole (**VI**)[6] is heated at 200°C with an equimolecular amount of o-aminothiophenol, in presence of triethylamine, the 2-(2′-amino-5′-ethoxycarbonyl-4′-thiazolyl)methylbenzothiazole (**VII**) is obtained.

The ^{1}H-nmr spectrum (DMSO-d_6) of **VII** shows signals at δ 1.05 ppm (t, 3H, CH_3), 4.05 (q, 2H, CH_2), 4.5 (s, 2H, CH_2), 7.35 (m, 2H, aromatic H-5 + H-6) and 7.85 (m, 4H, aromatic H-4 + H-7 + NH_2, exchange after D_2O). Its ir spectrum displays absorption bands at 3300, 3100 (NH), 1675 (CO) and 1645 cm^{-1} (NH_2).

Compound **VII** undergoes ring closure in refluxing sodium ethoxide solution to give **IV**.

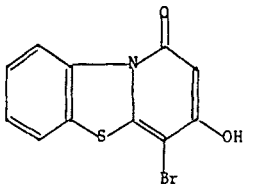


VI VII IV

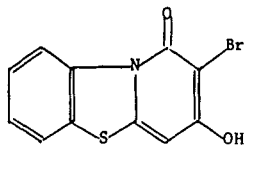
Moreover, compound **V** is independently prepared and found to be different from **IV** (See below).

In contrast to sulphuryl chloride, bromine reacts with **I** in acetic acid to yield the 4-bromo derivative **VIII**, rather than the 2-bromo isomer **IX**.

The assignment of structure **VIII** to the reaction product is based on: (a) Compound **VIII** reacts with thiourea to give **V** (see below). (b) The ^{1}H nmr spectrum (DMSO-d_6) of **VIII** shows signals at δ 5.75 (s, 1H, disappears after D_2O exchange, OH), 7.4 (m, 3H, aromatic H-7 & H-8 + ethylenic H-2), 7.9



VIII



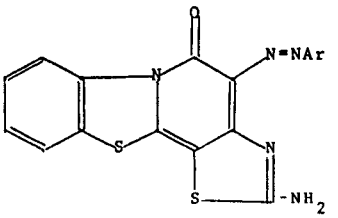
IX

(d, 1H, aromatic H-9), 8.9 (d, 1H, aromatic H-6). (c) Bromination of acetoacetanilides with bromine in acetic acid are known to yield the γ-bromo derivatives.[8,9]

Condensation of **VIII** with thiourea in boiling dioxane yields the 2-amino-5H-thiazolo[4′,5′: 4,3]pyrido[2,1-*b*]benzothiazol-5-one (**V**), with a new ring system.

Assignment of structure **V** to the reaction product is based on: (a) Compound **V** is different from **IV**. (b) The ^{1}H nmr (DMSO-d_6) of **V** shows signals at δ 7.08 (s, 1H, H-4), 7.6 (m, 2H, aromatic H-7 & H-8), 8.01 (m, 2H, aromatic H-6 & H-9), 9.2 (broad s, 2H, disappears after D_2O exchange, NH_2) and its ir spectrum displays absorption bands at 3100 (broad, NH) and 1660 cm^{-1} (CO).

Compound **V** couples with arenediazonium salts in pyridine, in presence of sodium hydroxide solution, to afford the 4-arylazo derivatives **X**.

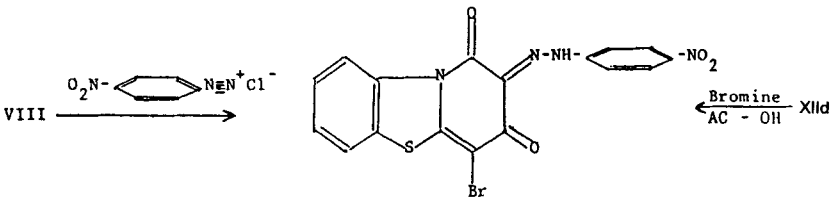


X	Ar
a	C_6H_5
b	C_6H_4Cl-p
c	$C_6H_4OCH_3$-p

X

The UV spectrum of **Xa** shows a maximum at 280 nm and its ir spectrum displays absorption bands characteristic for CO and NH groups.

Compound **VIII** couples with p-nitrobenzenedizonium chloride in ethanol in presence of sodium acetate to yield 4-bromo-2,3-dihydro-1H-pyrido[2,1-b]-benzothiazole-1,2,3-trione 2 · p-nitrophenylhydrazone (**XI**).

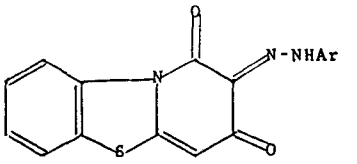


XI

The assignment of structure **XI** to the coupling product is based on: (a) Unlike azo compounds obtained from diazonium salts coupled with aliphatic carbon atom, which absorb strongly at about 280 nm, the uv spectrum of **XI** shows an absorption maximum at 470 nm, similar hydrazones are known to exhibit strong absorption at wavelengths higher than 320 nm.[9] (b) Compound **XI** can be

obtained by an alternative route (see below). (c) The ir spectrum of **XI** displays absorption bands at 3100 (NH), 1695 & 1670 cm^{-1} (2 CO).

Compound **I** couples with arenediazonium salts in ethanol in presence of sodium acetate to yield the corresponding 2-aryl-hydrazone derivatives, more properly represented as 2,3-dihydro-1H-pyrido[2,1-b]benzothiazole-1,2,3-trione 2-arylhydrazones (**XII**).



XII

XII	Ar
a	C_6H_5
b	C_6H_4Br-p
c	C_6H_4Br-o
d	$C_6H_4NO_2$-p

The assignment of structure **XII** to the coupling products is based on: the uv spectrum of **XIIa** shows an absorption maximum at 440 nm. (b) Bromination of **XIId** yields **XI** (See below). (c) The ir spectrum of **XII** displays two absorption bands in the carbonyl region.

Whereas bromination of **XIIa** with bromine in acetic acid leads to the formation of **XIIb** and **XIIc**, bromination of **XIId** under the same experimental conditions yields **XI**.

$$\textbf{XIIa} \xrightarrow[AcOH]{\text{Bromine}} \textbf{XIIb} + \textbf{XIIc}$$

EXPERIMENTAL

All melting points are uncorrected. IR spectra are recorded (KBr) on a Paye Unicam SP-1000 spectrophotometer. ^1H nmr spectra are obtained in $(CD_3)_2SO$ with a Varian EM-390 spectrometer with $SiMe_4$ as internal standard, and chemical shifts are expressed as δ values. Uv spectra are taken in dioxane and recorded on a Beckman DK spectrophotometer. Microanalytical data are performed by the Microanalytical Center at Cairo University. 3-Hydroxy-1H-pyrido[2,1-b]benzothiazol-1-one (**I**) is prepared by the method of Hawlitzky *et al.*[5]

2-Chloro-3-hydroxy-1H-pyrido[2,1-b]benzothiazol-1-one (**II**). Sulphuryl chloride (0.77 ml, 0.01 mol) is gradually added to a cold suspension of 2.17 g (0.01 mol) of **I** with stirring. After few minutes the solid has dissolved and precipitation takes place. The stirring is continued for 15 minutes, the precipitate is collected by filtration and crystallised from dilute acetic acid to give 2.01 g (80%); m.p. 255°C. Anal. Found (calcd.): C, 52.51 (52.49); H, 2.43 (2.40); Cl, 14.02 (14.10); N, 5.65 (5.57); S, 12.60 (12.71).

2-Amino-11H-thiazolo[4',5': 4,5]pyrido[2,1-b]benzothiazol-11-one (**IV**). A mixture of **II** (2.52 g, 0.01 mol), thiourea (0.84 g, 0.011 mol) and dioxane (50 ml) is refluxed for 3 h. The reaction mixture is allowed to cool, poured into water, the solid separated is collected, washed with water and crystallised from dimethylsulphoxide to give 1.77 g (65%), of **IV**, m.p. > 300°C.-ir (KBr): 3300, 3150 (NH), 1670 (CO), 1650 cm^{-1} (NH_2). Anal. Found (calcd.): C, 53.00 (52.74); H, 2.72 (2.58); N, 15.54 (15.39); S, 23.26 (23.43).

2-(2'-Amino-5'-ethoxycarbonyl-4'-thiazolyl)methylbenzothiazole (**VII**). A mixture of o-aminothiophenol (1.25 g, 0.01 mol), 2-amino-5-ethoxycarbonyl-4-ethoxycarbonylmethylthiazole (VI) (2.58 g, 0.01 mol) and a catalytic amount of triethylamine are heated at 200°C for 3 h. The reaction mixture is cooled and triturated with ethanol. The solid that separated is collected and crystallised from ethanol to give 1.60 g (50%) of **VII**; m.p. 208°C. Anal. Found (calcd.): C, 52.74 (52.65); H, 4.17 (4.11); N, 13.23 (13.17); S, 20.04 (20.05).

Cyclisation of **VII**.—*Preparation of* **IV**. A solution of 1 g of **VII** is dissolved in 25 ml of absolute ethanol containing about 0.2 g of sodium is refluxed for 16 h. The solution is evaporated to dryness and 50 ml of cold water are added. The solid that separated is collected and crystallised from dimethylsulphoxide to give 0.60 g (70%) of **IV**; m.p. > 300°C.—Identical ir spectra.

4-Bromo-3-hydroxy-1H-pyrido[2,1-b]benzothiazol-11-one. (**VIII**). To a solution of I (2.17 g, 0.01 mol) in 50 ml of acetic acid, bromine (0.51 ml, 0.01 mol) in 20 ml of acetic acid is gradually added with shaking. The reaction solution is heated on a water bath for 30 minutes, left to cool and poured into water. The white precipitate is collected, washed thoroughly with water, dried and crystallised from dimethylformamide; to give 2.07 g (70%) of **VIII**; m.p. 260°C—ir (KBr): 3100 (OH), 2750 (CH), 1670 cm^{-1} (CO). Anal. Found (calcd.): C, 44.80 (44.61); H, 2.22 (2.04); Br, 26.95 (26.98); N, 4.70 (4.73); S, 10.94 (10.83).

2-Amino-5H-thiazolo[4',5': 4,3]pyrido[2,1-b]benzothiazol-5-one (**V**). A mixture of **VIII** (2.96 g, 0.01 mol), thiourea (0.83 g, 0.011 mol), and dioxane (100 ml), is refluxed for 3 h. The reaction mixture is cooled and poured into cold water. The solid that separated is filtered off, dried and crystallised from dimethylsulphoxide to give 1.77 g (65%) of **V**; m.p. > 300°C. Anal. Found (calcd.): C, 52.95 (52.74); H, 2.73 (2.58); N, 15.27 (15.39); S, 23.33 (23.43).

2-Amino-4-arylazo-5H-thiazolo[4',5': 4,3]pyrido[2,1-b]benzothiazol-5-one (**Xa–c**). General procedure: About 1 g of **V** is dissolved in 40 ml of pyridine containing 2 ml of 10% sodium hydroxide solution, cooled in an ice bath, and treated with an equimolecular amount of the appropriate diazotized amine, prepared by the diazotisation of the calculated amount of the corresponding amine in 10 ml of hydrochloric acid with sodium nitrite solution. The mixture is left for 2 h and then diluted with cold water. The buff precipitate is collected, dried and washed with hot dimethylformamide to give **X** (c.f. Table I). The uv (dioxane) spectrum of Xa shows maxima at 280 (ϵ15.500), 240 nm (ϵ8,700).

4-Bromo-2,3-dihydro-1H-pyrido[2,1-b]benzothiazole-1,2,3-trione 2-p-nitrophenylhydrazone (**XI**). Method A: 1.48 g (0.005 mol) of **VIII** is suspended in 50 ml of ethanol containing 0.5 g of sodium acetate, cooled in an ice bath, and treated with an equimolecular amount of diazotised p-nitroaniline, prepared by the diazotisation of 0.69 g (0.005 mol) of p-nitroaniline in 10 ml of hydrochloric acid with sodium nitrite solution. The mixture is left for 1 h and then diluted with cold water. The precipitate is collected, dried and crystallised from dimethylsulphoxide to yield **XI** in 75% yield; m.p. > 300°C. The uv (dioxane) of **XI** shows maxima at 470 (ϵ38.400) and 295 nm (ϵ14.200). Anal. Found (calcd.): C, 46.04 (45.85); H, 2.11 (2.03); Br, 17.99 (17.95); N, 12.45 (12.59); S, 7.20 (7.19).

Method B: Bromine solution (0.26 g, 0.005 mol in 20 mol of acetic acid) is added gradually to a solution of **XIId** (1.83 g, 0.005 mol) and a similar procedure as that mentioned for bromination of **I** is followed to yield **XI** in 65% yield; m.p. > 300°C.—Identical ir spectra.

2,3-Dihydro-1H-pyrido[2,1-b]benzothiazole-1,2,3-trione 2-arylhydrazones (**XII**). General procedure: About 2 g of **I** is suspended in 50 ml of ethanol containing 1 g of sodium acetate, cooled in an ice bath, and treated with an equimolecular amount of the appropriate diazotised amine. The mixture is left for 1 h and then diluted with water. The red precipitate is collected, dried and crystallised from the proper solvent (c.f. Table II). The ^{1}H nmr spectrum (DMSO-d_6) of **XIIa** shows signals at δ 6.35

TABLE I

2-Amino-4-arylazo-5H-thiazolo[4',5': 4,3]pyrido[2,1-b]benzothiazol-5-one (**X**)

Comp.* no.	M.P. °C	Yield %	Ar	Formula (M.W.)	Analysis calcd/found C	H	N	S	Cl
Xa	>300	85	C_6H_5	$C_{18}H_{11}N_5OS_2$ (377)	57.28 57.41	2.94 3.12	18.57 18.70	16.97 16.84	
Xb	>300	80	C_6H_4Cl-p	$C_{18}H_{10}ClN_5OS_2$ (412)	52.49 52.65	2.44 2.53	17.03 17.00	15.55 15.50	8.61 8.51
Xc	>300	80	$C_6H_4OCH_3$-p	$C_{19}H_{13}N_5O_2S_2$ (407)	56.01 56.23	3.21 3.30	17.20 17.11	15.72 15.65	

* Ir spectra (KBr) for **Xa–c** display absorption bands around 3300 & 3150 (NH), 1660 (CO).

TABLE II
2,3-Dihydro-1H-pyrido[2,1-b]benzothiazole-1,2,3-trione 2-arylhydrazones (**XII**)

Comp.* no.	M.P.°C. Solvent	Yield %	Ar	Formula (M.W.)	Analysis calcd./found C	H	N	S	Br
XIIa	252	85	C_6H_5	$C_{17}H_{11}N_3O_2S$	63.54	3.45	13.09	9.96	
	AcOH			(321)	63.59	3.55	13.17	9.90	
XIIb	263	80	C_6H_4Br-p	$C_{17}H_{10}BrN_3O_2S$	51.01	2.52	10.51	8.00	19.97
	DMF			(400)	51.17	2.50	10.57	7.91	20.15
XIIc	>300	76	C_6H_4Br-o	$C_{17}H_{10}BrN_3O_2S$	51.01	2.52	10.51	8.00	19.97
	AcOH			(400)	51.02	2.44	10.61	7.90	19.85
XIId	>300	70	$C_6H_4NO_2$-p	$C_{17}H_{10}N_4O_4S$	55.73	2.75	15.31	8.74	
	DMF			(366)	55.81	2.81	15.15	8.66	

* Ir spectra (KBr) for **XIIa–d** display absorption bands around 3200 (NH), 1700 & 1680 cm^{-1} (2 CO).

(s, 1H, H-4), 7.55 (m, 9H, aromatic protons), 8.70 (broad s, 1H, disappears after D_2O exchange, NH). Its uv (dioxane) shows maxima at 412 (ϵ35.500), 320 nm (ϵ11.500).

Bromination of **XIIa**. Preparations of **XIIb** & **XIIc**.—Method B: To a solution of **XIIa** (1.6 g, 0.005 mol) in 40 ml of acetic acid, bromine (0.26 ml, 0.005 mol) in 20 ml of acetic acid is gradually added with shaking. Shaking and heating on a water bath is continued for 1 h. The reaction mixture is left to cool, whereupon precipitation of **XIIb** occurs, the precipitate is collected and crystallised from dimethylformamide to give 1 gm (50%) of **XIIb**; m.p. and mixed m.p. 263°C. The filtrate, after separation of **XIIb**, is diluted with water to precipitate **XIIc**, which is collected and crystallised from acetic acid to give 0.6 gm (30%) of **XIIc**; m.p. > 300°C.—Identical ir spectra.

REFERENCES

1. A. M. Abdel-Fattah, S. M. Hussain and A. M. El-Reedy, *J. Heterocyclic Chem.*, **19,** 1341 (1982).
2. H. A. Hammouda, A. M. El-Reedy, M. A. F. Sharaf and A. M. Abdel-Fattah, *J. Heterocyclic Chem.*, **21,** 337 (1984).
3. A. M. Abdel-Fattah, A. M. El-Reedy, S. M. Hussain and A. H. Ibrahim, *Indian J. Chem.*, **22B,** 555 (1983).
4. A. M. Abdel-Fattah, S. M. Hussain and M. I. Ali, *Tetrahedron*, **30,** 987 (1974).
5. N. Hawlitzky, R. Haller and K. W. Mertz, *Arch. Pharm.*, **301,** 17 (1968).
6. J. M. Sprague, R. M. Lincoln and C. Ziegler, *J. Am. Chem. Soc.*, **68,** 266 (1946).
7. D. J. Cook, R. E. Bowen, P. Sorter and E. Daniels, *J. Org. Chem.*, **26,** 4949 (1961).
8. R. J. Chudgar and K. N. Trivedi, *Curr. Sci. (India)*, **34,** 560 (1965).
9. H. C. Yao and P. Resnick, *J. Am. Chem. Soc.*, **84,** 3514 (1962).