Thieno[2,3-*b*]pyridines and Thieno[3,2-*b*]pyridines by the Method of Gould-Jacobs

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Bis(2-, and 3-thienylammonium) hexachlorostannates were condensed with ethoxymethylene derivatives of active methylene compounds in pyridine. The resulting condensation products IVa-IVc and Va-Vc on heating under reflux in Dowtherm or diphenyl ether provided various 4-hydroxythieno[2,3-*b*]pyridines (Ia-Ic) and 7-hydroxythieno[3,2-*b*]pyridines (IIa-IIc). The compound Ic on further transformations gave yet other derivatives If-Ik.

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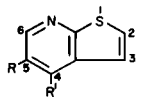
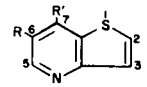
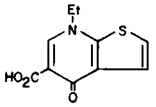
Various thieno[2,3-*b*]pyridines and thieno[3,2-*b*]pyridines have previously been obtained from 2-, or 3-aminothiophene salts by Skraup's synthesis (2) or by their reactions with 1,3-dicarbonyl compounds (3), or methyl vinyl ketone (4). Other derivatives of these thienopyridines were obtained by subjecting them to appropriate substitution reactions (5). A recent review has covered the chemistry of thienopyridines (6). There is no report of the application of Gould-Jacobs method (7) for the synthesis of these systems (8). Application of this method would lead to 5-substituted-4-hydroxythieno[2,3-*b*]pyridines (I) and 6-substituted-7-hydroxythieno[3,2-*b*]pyridines (II). This synthesis can also lead to 4,7-dihydro-7-ethyl-4-oxo-7*H*-thieno[2,3-*b*]pyridine-5-carboxylic acid (III), an isostere of the antibacterial agent nalidixic acid (9). Our interest in the synthetic applications of Gould-Jacobs reaction led us to utilize ethoxymethylene derivatives of various active methylene compounds for the synthesis of several thienopyridines I and II.



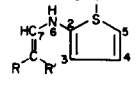
Ia R = CN, R′ = OH
Ib R = COMe, R′ = OH
Ic R = CO_2Et, R′ = OH
Id R = COMe, R′ = Me
Ie R = CN, R′ = Cl
If R = CO_2H, R′ = OH
Ig R = CO_2Et, R′ = OMe
Ih R = CO_2H, R′ = OMe
Ii R = H, R′ = OH
Ij R = H, R′ = Cl
Ik R = CO_2Et, R′ = Cl



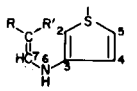
IIa R = CN, R′ = OH
IIb R = COMe, R′ = OH
IIc R = CO_2Et, R′ = OH



III



IVa R = CN, R′ = CO_2Et
IVb R = COMe, R′ = CO_2Et
IVc R = CO_2Et, R′ = CO_2Et
IVd R = COMe, R′ = COMe



Va R = CN, R′ = CO_2Et
Vb R = COMe, R′ = CO_2Et
Vc R = CO_2Et, R′ = CO_2Et
Vd R = COMe, R′ = COMe

Reductions of 2-nitrothiophene (10) and 3-nitrothiophene (11) were effected by means of tin and hydrochloric acid (12) and the corresponding bis(2-, and 3-thienylammonium) hexachlorostannates were isolated and used without further purification.

When bis(2-thienylammonium) hexachlorostannate was allowed to react with ethyl ethoxymethylenecyanoacetate in an ethanolic solution under reflux, no condensation product was isolated. Various attempts to effect condensation under these conditions were unsuccessful. Next attempts were directed to bring about this condensation using "free" 2-aminothiophene. As the free 2-aminothiophene is not very stable, being readily polymerized (13), the condensation of the amine, liberated *in situ*, with ethyl ethoxymethylenecyanoacetate was attempted. On the basis of these results (Table I) bis(2-, and 3-thienylammonium) hexachlorostannates were condensed with ethoxymethylene derivatives of other active methylene compounds in pyridine at 40-50° over a period of 24 hours.

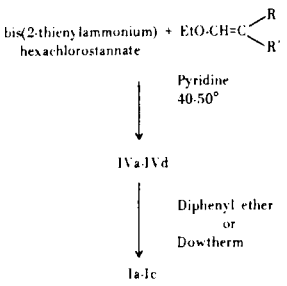
Table I

Attempted Condensations of Bis(2-thienylammonium) Hexachlorostannate with Ethyl Ethoxymethylenecyanoacetate

Solvent	Temperature °C	Time, hours	Yield of IVa %
Ethanol	78	2	none
5% Ethanolic Sodium Hydroxide	78	2	none
Ethanol-Pyridine (97:3)	28	0.5	traces
Ethanol-Pyridine (97:3)	78	0.5	3
Pyridine	100	2	17
Pyridine	28	48	50
Pyridine	40-50	24	88

Scheme I outlines the general route for the synthesis of 5-substituted-4-hydroxythieno[2,3-*b*]pyridines (Ia-Ic). Following Scheme I but using bis(3-thienylammonium) hexachlorostannate, instead of bi(2-thienylammonium)

Scheme I



hexachlorostannate, 6-substituted-7-hydroxythieno[3,2-*b*]-pyridines (IIa-IIc) were obtained.

All the 2-, and 3-(*N*-thienyl)aminomethylene compounds (IVa-IVd and Va-Vd) obtained are listed in Table II. The condensation products of the Table II were identified by spectral analyses (Tables III and IV). The cyclizations to the corresponding I(a-c) or II(a-c) were effected either in refluxing Dowtherm or in diphenyl ether. The compounds IVd and Vd could not be cyclized under these conditions nor with sulfuric or polyphosphoric acids. However, heating with phosphoryl chloride IVd gave the desired cyclized product Id which was characterized as its 2,4-dinitrophenyl hydrazone. Various I and II obtained in these cyclizations are listed in Table V and their spectral data in the Tables VI and VII together with those of other thieno[2,3-*b*]pyridines (Id-Ik) prepared during the present work.

The pmr spectra of the two isomeric thienopyridines were consistent with their structure and in accord with the data of other thienopyridines reported by Klemm, *et al.* (3b,5).

The carbonyl group of 5-acetylthieno[2,3-*b*]pyridine and 6-acetylthieno[3,2-*b*]pyridine is reported to absorb at 1690 cm^{-1} and that of the 5-carbomethoxythieno[2,3-*b*]-pyridine at 1720 cm^{-1} in the infrared spectrum (3b,5). In the present work compounds Ib and IIb showed the carbonyl absorption for the acetyl group at 1660 and 1670 cm^{-1}, respectively: for the ester group in Ic and IIc at 1700 cm^{-1}, in Ig and Ik at 1710 cm^{-1}; and for the acids If and Ih at 1650 and 1710 cm^{-1}, respectively. A broad band between 3200 and 2500 cm^{-1} was also observed for all these compounds. The shift to the longer wavelength of the infrared absorption bands in the esters (Ic, IIc, Ig and Ik), ketones (Ib and IIb), and the acids (If and Ih) is ascribed as due to the intramolecular hydrogen bonding with the 4-, or 7-hydroxy groups at the adjacent positions.

In contrast to Klemm and Hartling's recently reported 6-hydroxythieno[2,3-*b*]pyridine which exists predominately as the pyridone, indicated by the absorption bands at 3440 cm^{-1} (NH) and at 1640 cm^{-1} (carbonyl) in the infrared spectrum (14), the 4-hydroxy compound Ii obtained during the present work exists possibly in the hydroxy form since it was devoid of characteristic absorption bands exhibited by its 6-hydroxy counterpart (see Table VI). This also confirms that the compound obtained by Klemm and Hartling was the 6 isomer as correctly reported by them (14).

In the pmr spectra of these compounds the proton α to the pyridine nitrogen appears as a sharp singlet between δ 8.16 and 8.75. Only in the case of IVc the proton α to the nitrogen appears at δ 9.25 (the solvent used for the pmr spectrum was deutrotrifluoroacetic acid which caused this downfield shift).

On the basis of these spectral evidence it is assumed that the various hydroxythienopyridines reported here exist in this rather than in the pyridone form and are tentatively represented here as the hydroxy tautomers.

Some transformations of Ic and Ia were carried out to provide other derivatives of thieno[2,3-*b*]pyridine. Thus Ic was hydrolyzed to afford the corresponding acid If and alkylation of this acid with ethyl iodide in base gave the *N*-alkylated product III. While on alkylation of Ic with diazomethane an *O*-alkylated compound Ig was obtained. Decarboxylation of If gave the compound Ii which on treatment with phosphoryl chloride afforded Ij. A similar treatment of Ic gave Ik. The compound Ig on hydrolysis gave the methoxy acid Ih. Ie was obtained from Ia by chlorination with phosphoryl chloride.

EXPERIMENTAL

All melting points are uncorrected. Pmr spectra were taken on a 60 MHz Hitachi Perkin-Elmer R-20b using tetramethylsilane as an internal standard. Ir spectra were measured on Perkin-Elmer model 180 and the elemental analysis on Perkin-Elmer 240. The organic extracts were dried on anhydrous magnesium sulfate.

The following starting materials were prepared according to the literature method: ethyl ethoxymethylenecyanoacetate, b.p. 169°/17 mm (15); ethyl ethoxymethyleneacetoacetate, b.p. 149-151°/16 mm (16); ethoxymethyleneacetylacetone, b.p. 138-141°/16 mm (17); 2-nitrothiophene, m.p. 44-45° (10); 3-nitrothiophene, m.p. 75° (11) and bis(2-, and 3-thienylammonium) hexachlorostannates (12). Diethyl ethoxymethylenemalonate and other reagents were commercial products and were used without purification.

Condensations of Bis(2-, or 3-thienylammonium) Hexachlorostannates with Various Ethoxymethylene Compounds.

The following procedure for the condensation of bis(2-thienylammonium) hexachlorostannate with ethyl ethoxymethylenecyanoacetate represents the general method used for the condensations. The products of these condensations are listed in Table II and their spectral data in Tables III and IV.

Ethyl α-Cyano-β-(*N*-2-thienyl)aminoacrylate (IVa).

To a stirring solution of 12.7 g. (0.075 mole) of ethyl ethoxymethylenecyanoacetate in 200 ml. of pyridine, there was added, portionwise, 20 g. (0.038 mole) of bis(2-thienylammonium) hexachlorostannate. The reaction mixture was stirred for 24 hours at 40-45° and then poured onto 500 g. of crushed ice, added sufficient ammonia till *p*H 11 and extracted with chloroform (3 x 200

Table II

N-(2-, and 3-Thienyl)aminomethylene Compounds (IVa-IVd and Va-Vd)

Compound No.	Ethoxymethylene Compound (a)	Yield %	M.p. °C	Crystallization Solvent (b)	Formula	Analyses (c) % C	H	N
IVa	EMCA	88	93-95	A	$C_{10}H_{10}N_2O_2S$	54.09 (54.04)	4.69 (4.53)	12.65 (12.60)
IVb	EMAE	84	77-78	A	$C_{11}H_{13}NO_3S$	55.07 (55.21)	5.73 (5.48)	6.13 (5.85)
IVc	EMME	80	45-46	B	$C_{12}H_{15}NO_4S$	53.70 (53.52)	5.73 (5.61)	5.21 (5.20)
IVd	EMAA	60	108	C	$C_{10}H_{11}NO_2S$	57.40 (57.41)	5.47 (5.26)	6.69 (6.69)
Va	EMCA	68	122-123	C	$C_{10}H_{10}N_2O_2S$	54.13 (54.04)	4.54 (4.53)	12.36 (12.60)
Vb	EMAE	50	58-59	C	$C_{11}H_{13}NO_3S$	55.50 (55.21)	5.52 (5.48)	5.55 (5.85)
Vc	EMME	70	74-75	A	$C_{12}H_{15}NO_4S$	53.34 (53.52)	5.43 (5.61)	4.95 (5.20)
Vd	EMAA	69	99-100	C	$C_{10}H_{11}NO_2S$	57.29 (57.41)	5.19 (5.26)	6.72 (6.69)

(a) EMCA, ethyl ethoxymethylenecyanoacetate; EMAE, ethyl ethoxymethyleneacetoacetate; EMME, diethyl ethoxymethylenemalonate; EMAA, ethoxymethyleneacetylacetone. (b) A, hexane; B, ether/petroleum ether (b.p. 40-60°); C, heptane. (c) Figures in parentheses represent calculated values.

Table III

Spectroscopic Properties of 2-Thienylaminomethylene Compounds (IVa-IVd)

Compound No.	Pmr (a) H-3	H-4	H-5	H-6	H-7	Coupling constants (Hz) $J_{3,4}$	$J_{4,5}$	$J_{6,7}$	Other signals	Ir (b) cm^{-1}
IVa	6.89	6.69	6.89	10.76	7.57	3.75	5.25	12.05	1.32 (t, CH_3), 4.29 (q, CH_2), J = 7.50	3200 (NH); 2215 (C≡N); 1705; 1670 (C=O)
IVb	6.87	6.70	6.87	13.50	8.13	4.50	5.25	11.25	1.32 (t, CH_3), 4.23 (q, CH_2), J = 7.50, 2.49 (s, CH_3)	3120 (NH); 1709; 1629 (C=O)
IVc	6.82	6.65	6.82	11.50	8.18	3.75	5.25	13.20	1.29 (t, CH_3), 1.32 (t, CH_3), 4.20 (q, CH_2), 4.27 (q, CH_2), J = 7.50	3240, 3080 (NH), 1689 (C=O)
IVd	6.89	6.72	6.89	12.96	7.90	4.80	5.20	12.00	2.29 (s, CH_3), 2.47 (s, CH_3)	3100 (NH), 1619 (C=O)

(a) Chemical shifts in δ; solvent deuteriochloroform. (b) Taken in potassium bromide pellets.

ml.). After removal of the solvent, the residue was chromatographed over alumina using benzene-ether (50%) as the eluting solvent. The product obtained from the chromatography was crystallized from hexane as yellow crystals, m.p. 83-87°. Recrystallization from hexane (activated charcoal) gave 14.7 g. (88%) of IVa, m.p. 93-95°.

Cyclizations of Ethyl α-Substituted-β-(*N*-2-, and *N*-3-thienyl)aminoacrylates.

The cyclizations of ethyl α-cyano-β-(*N*-2-thienyl)aminoacrylate (IVa) described below represents the general method for the cyclizations of the acrylates of Table II. Ia-Ic and IIa-IIc thus obtained are presented in the Table V and their spectra in the Tables VI and VII, respectively.

Table IV

Spectroscopic Properties of 3-Thienylaminomethylene Compounds (Va-Vd)

Compound No.	Pmr (a) H-2	H-4	H-5	H-6	H-7	Coupling constants (Hz) $J_{4,5}$	$J_{6,7}$	Other signals	Ir (b) cm^{-1}
Va	6.95	7.02	7.30	13.0	7.85	6.0	13.0	1.4 (t, CH_3), 4.4 (q, CH_2), J = 7.5	3110; 3080 (NH); 2205 (C≡N); 1705; 1670 (C=O)
Vb	7.00	7.04	7.25	13.0	8.20	6.0	12.6	1.4 (t, CH_3), 4.3 (q, CH_2), J = 7.5, 2.65 (s, CH_3)	3120 (NH); 1705; 1632 (C=O)
Vc	6.88	6.95	7.15	11.5	8.32	6.0	13.0	1.3 (t, CH_3), 1.35 (t, CH_3), 4.22 (q, CH_2), 4.32 (q, CH_2), J = 7.5	3100 (NH); 1710; 1648 (C=O)
Vd	7.03	7.10	7.30	13.0	8.20	6.0	12.0	2.4 (s, CH_3), 2.6 (s, CH_3)	3100; 3080 (NH); 1620 (C=O)

(a) Chemical shifts in δ; solvent deuteriochloroform. (b) Taken in potassium bromide pellets.

Table V

4-Hydroxythieno[2,3-*b*]pyridines (Ia-Ic) and 7-Hydroxythieno[3,2-*b*]pyridines (IIa-IIc) (a)

Compound No.	Yield %	M.p. °C	Sublimation	Formula	Analyses (b) % C	H	N
Ia	78	>300	160°/3 mm	$C_8H_4N_2OS$	54.75 (54.53)	2.41 (2.29)	15.80 (15.90)
Ib	63	184-185	100°/0.3 mm	$C_9H_7NO_2S$	56.26 (55.94)	3.84 (3.65)	7.33 (7.25)
Ic	60	160-161	110°/0.4 mm	$C_{10}H_9NO_3S$	53.88 (53.81)	4.18 (4.04)	6.42 (6.28)
IIa	80	>300	160°/16 mm	$C_8H_4N_2OS$	54.44 (54.53)	2.46 (2.29)	15.95 (15.90)
IIb	50	178-179	150°/4 mm	$C_9H_7NO_2S$	56.27 (55.94)	3.73 (3.65)	7.16 (7.25)
IIc	74	152-153	160°/16 mm	$C_{10}H_9NO_3S$	53.93 (53.81)	4.00 (4.04)	6.10 (6.28)

(a) Compounds Ia-Ic and IIa-IIc were obtained from the compounds IVa-IVc and Va-Vc, respectively. (b) Figures in parentheses represent calculated values.

5-Cyano-4-hydroxythieno[2,3-*b*]pyridine (Ia).

A mixture of 9 g. (0.04 mole) of IVa and 200 ml. of diphenyl ether was heated under reflux for 1.5 hours and after cooling was diluted with 500 ml. of petroleum ether (b.p. 40-60°) when a dark solid precipitated. This solid was filtered, washed with petroleum ether (b.p. 40-60°) and crystallized from 50% *N,N*-dimethylformamide-water (activated charcoal) giving Ia as yellow needles, m.p. >300°, yield, 5.5 g. (78%).

The samples for elemental analyses were prepared by sublimations at reduced pressure (Table V).

5-Acetyl-4-methylthieno[2,3-*b*]pyridine (Id).

A mixture of 2 g. (0.01 mole) of 3′-(*N*-2-thienyl)aminomethylenepentane-2′,4′-dione (IVd) and 20 ml. of phosphoryl chloride was heated under reflux for 2 hours. The reaction mixture after cooling was poured onto ice (500 g.), made alkaline with sodium hydroxide and extracted with chloroform (3 x 150 ml.). On removal of the solvent a dark colored solid was obtained which resisted crystallization. The yield of this crude product was 1.4 g. (77%). This was identified as its 2,4-dinitrophenyl hydrazone, m.p. 200-201° (ethanol).

Table VI

Spectroscopic Properties of Thieno[2,3-*b*]pyridines (Ia-Ik)

Compound No.	Pmr (a) H-2	H-3	H-5	H-6	Coupling Constants (Hz) $J_{2,3}$	$J_{5,6}$	Other signals	Solvent	Ir (b) cm^{-1}
Ia	7.40	7.40		8.52				DMSO-d_6	2219 (C≡N)
Ib	7.42	7.28		8.51	6.0		2.55 (s, CH_3)	DMSO-d_6	1660 (C=O)
Ic	7.40	7.18		8.40	6.0		1.80 (t, CH_3), 4.10 (q, CH_2) J = 7.5	DMSO-d_6	1700 (C=O)
Id (c)	7.75	7.35		8.20	6.0		2.67 (s, CH_3), 2.47 (s, CH_3), 8.91, 8.30, 7.85 (2,4-DNPH)	DMSO-d_6	3300 (NH); 1510, 1355 (NO_2)
Ie	7.75	7.50		8.69	6.0			deuteriochloroform	2240 (C≡N)
If	7.55	7.40		8.75	6.0			DMSO-d_6	1650 (C=O)
Ig	7.32	7.32		8.71			1.40 (t, CH_3), 4.35 (q, CH_2) J = 7.5, 4.05 (s, CH_3)	carbon tetrachloride	1710 (C=O)
Ih	7.86	7.62		8.75	6.0		4.15 (s, CH_3)	DMSO-d_6	1710 (C=O)
Ii	7.52	7.35	6.60	8.16	6.0	6.0		DMSO-d_6	3200-2500 (br., OH) (d)
Ij	7.55	7.32	7.25	8.40	6.0	5.0		deuteriochloroform	
Ik	7.57	7.42		8.92	6.0		1.38 (t, CH_3) 4.30 (q, CH_2) J = 7.5	deuteriochloroform	1710 (C=O)

(a) Chemical shifts in δ; (b) Taken in potassium bromide pellets; (c) As 2,4-dinitrophenylhydrazone (DNPH); (d) No absorption bands above 1600 cm^{-1}.

Table VII

Spectroscopic Properties of Thieno[3,2-*b*]pyridines (IIa-IIc)

Compound No.	Pmr (a) H-2	H-3	H-5	Coupling Constant (Hz) $J_{2,3}$	Other Signals	Solvent	Ir (b) cm^{-1}
IIa	8.15	7.30	8.60	6.0		DMSO-d_6	2215 (C≡N)
IIb	8.05	7.35	8.45	6.0	2.65 (s, CH_3)	DMSO-d_6	1670 (C=O)
IIc	8.50	7.80	9.25	6.0	1.55 (t, CH_3), 4.70 (q, CH_2) J = 7.5 Hz	TFA	1700 (C=O)

(a) Chemical shifts in δ; (b) Taken in potassium bromide pellets; broad absorption bands in the region 3200-2500 cm^{-1}.

Anal. Calcd. for $C_{16}H_{13}N_5O_4S$: C, 51.75; H, 3.53; N, 18.86. Found: C, 52.20; H, 3.86; N, 18.58.

4-Chloro-5-cyanothieno[2,3-*b*]pyridine (Ie).

A mixture of 1 g. (0.006 mole) of Ia and 5 ml. of phosphoryl chloride was heated under reflux for 2 hours and after cooling was poured onto crushed ice (200 g.). On filtration a white solid melting at 100-105° was obtained which was crystallized from ethanol and further purified by sublimation giving Ie, m.p. 120°, as colorless crystals, yield 0.83 g. (76%).

Anal. Calcd. for $C_8H_3ClN_2S$: C, 49.38; H, 1.55; N, 14.39. Found: C, 49.21; H, 1.66; N, 14.48.

4-Hydroxythieno[2,3-*b*]pyridine-5-carboxylic Acid (If).

A mixture of 3 g. (0.013 mole) of Ic in 10% sodium hydroxide (30 ml.) was heated under reflux for 0.5 hours. At the end of this period activated charcoal was added to the mixture and heated for a few more minutes and filtered. The filtrate was acidified with sulfuric acid and the precipitated acid was filtered, washed with cold water and crystallized from boiling water giving If as colorless crystals, m.p. 238-239°, yield 2.4 g. (92%).

Anal. Calcd. for $C_8H_5NO_3S$: C, 49.23; H, 2.58; N, 7.18. Found: C, 49.18; H, 2.67; N, 6.93.

4,7-Dihydro-7-ethyl-4-oxo-7*H*-thieno[2,3-*b*]pyridine-5-carboxylic Acid (III).

To a hot solution of 0.59 g. of potsasium hydroxide in 12 ml. of ethanol and 4 ml. of water, there was added 0.58 g. (0.003 mole) of If. After the acid had completely dissolved there was added 1.4 ml. of ethyl iodide and the mixture was heated under reflux for 50 hours, chilled in an ice bath, filtered and washed with ice-cold water. After recrystallization from dimethyl sulfoxide-water, 0.35 g. (52%) of III, m.p. 268°, was obtained as colorless crystals; pmr δ (DMSO-d_6): 8.83 (s, H-6), 7.65 (d, H-2), 7.53 (d, H-3), $J_{2,3}$ = 6 Hz and 4.40 (q), 1.50 (t) (*N*-Et, J = 7.5 Hz); ir (potassium bromide pellet): 1700 cm^{-1} (carbonyl).

Anal. Calcd. for $C_{10}H_9NO_3S$: C, 53.80; H, 4.06; N, 6.27. Found: C, 53.57; H, 3.93; N, 6.16.

Ethyl 4-Methoxythieno[2,3-*b*]pyridine-5-carboxylate (Ig).

To a solution of 2.3 g. (0.01 mole) of Ic in chloroform (50 ml.), there was added a solution of diazomethane in ether, a vigorous reaction took place with the evolution of nitrogen. The reaction mixture was left overnight at room temperature. After evaporation of the solvent a red syrup was obtained which was crystallized from heptane giving Ig as yellow colored crystals, m.p. 40-41°, yield 1.5 g. (63%).

Anal. Calcd. for $C_{11}H_{11}NO_3S$: C, 55.68; H, 4.67; N, 5.90. Found: C, 56.12; H, 4.73; N, 5.86.

4-Methoxythieno[2,3-*b*]pyridine-5-carboxylic Acid (Ih).

A mixture of 1.2 g. (0.005 mole) of Ig and 19 ml. of 6% sodium hydroxide solution was stirred at room temperature for 10 hours, filtered and acidified with hydrochloric acid giving a solid which on crystallization from water afforded Ih, m.p. 160°, yield 0.7 g. (66%).

Anal. Calcd. for $C_9H_7NO_3S$: C, 51.67; H, 3.37; N, 6.70. Found: C, 51.38; H, 3.35; N, 6.51.

4-Hydroxythieno[2,3-*b*]pyridine (Ii).

This compound was obtained as a light brown solid, m.p. 219°, when 1 g. (0.005 mole) of If was heated under reflux in 20 ml. of Dowtherm for 1 hour and after cooling precipitated with pentane. Compound Ii was purified by sublimation, yield 0.65 g. (84%).

Anal. Calcd. for C_7H_5NOS: C, 55.61; H, 3.33; N, 9.27. Found: C, 55.95; H, 3.37; N, 8.84.

4-Chlorothieno[2,3-*b*]pyridine (Ij).

A mixture of 0.3 g. (0.002 mole) of Ii and 2 ml. of phosphoryl chloride was heated under reflux for 2 hours. After cooling, the reaction mixture was poured onto crushed ice (50 g.), basified with ammonia and extracted with methylene chloride (3 x 20 ml.). The solvent was removed and the residue was crystallized from heptane giving Ij, m.p. 31-32°; lit. m.p. 56.8-58.5° (14), yield 0.27 g. (83%).

Anal. Calcd. for C_7H_4ClNS: C, 49.56; H, 2.34; N, 8.26. Found: C, 49.69; H, 2.52; N, 8.03.

Ethyl 4-Chlorothieno[2,3-*b*]pyridine-5-carboxylate (Ik).

This ester was obtained in a similar manner as Ie by treating 2.23 g. (0.01 mole) of Ic with 2 ml. of phosphoryl chloride. It crystallized from pentane, m.p. 69-70°, yield 1.83 g. (76%).

Anal. Calcd. for $C_{10}H_8ClNO_2S$: C, 49.69; H, 3.31; N, 5.79. Found: C, 49.69; H, 3.34; N, 5.80.

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