# Chemistry of Thienopyridines. VII. Mechanistic Studies on the Synthesis of Thieno[2,3-c]pyridine by Thermolytic Cyclization (1)

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A study was made of the formation of thieno[2,3-c]pyridine (1) from hydrogen sulfide and 4-vinylpyridine in a flow system at 630°. 2-(4-Pyridyl)ethanethiol and bis-2-(4-pyridyl)ethyl sulfide were found to be likely intermediates. Based on these studies, there was devised a two-step practical preparative method for 1 (optimum overall yield 58%) which consists of preliminary conversion of 4-vinylpyridine to benzyl 2-(4-pyridyl)ethyl sulfide and subsequent thermolysis (at 605°) of this substance.

Thieno[2,3-c]pyridine (1) was first synthesized in very low yield (4%) from thiophene-2-aldehyde by Herz and Tsai (5) by means of the Pomeranz-Fritsch reaction. Hansch, Carpenter, and Todd (6) next synthesized 1 by a seven-step procedure from 4-ethylpyridine (3% overall yield), wherein the last step (effected in 50% yield) involved the dehydrocyclization of 4-ethylpyridine-3-thiol in the presence of copper chromium oxide on charcoal at 425°. An attempt by Hansch and Carpenter (7) to prepare 1 in a single step from the available 4-vinylpyridine (4-VPy)
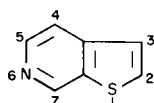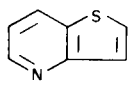
by reaction with hydrogen sulfide in the presence of sulfided iron-aluminum oxides at 600° failed. Instead of 1, these authors isolated bis-2-(4-pyridyl)ethyl sulfide (III, 18% crude yield) as the only ether-soluble identified product. In contrast to the observations of Hansch and Carpenter, Klemm and Reed (8) obtained thieno[3,2-b]-pyridine (VII, 2% yield) from 2-vinylpyridine (2-VPy) under similar conditions. The 3-vinylpyridine-hydrogen sulfide system also gave low yields of thienopyridines (9, 10). The present paper describes the successful conversion of 4-vinylpyridine to 1 in 58% overall yield by a two-step process (11) (or in lower yield by a one-step process). Thus, for the first time, 1 has become available in sufficient quantities to allow extensive investigation of its chemical and physical properties.

Attempts to prepare 1 by interaction of 4-VPy and hydrogen sulfide were modeled after the procedures of Moore and Greensfelder (12), Patterson et al. (13), and Venuto, Landis, and Boswell (14) for conversion of styrene to benzo[b]thiophene at 500-665° (optimal 600-635°) in

the presence of sulfided metal oxides (e.g. alumina, chromia-alumina, iron oxide-alumina). Moore and Greensfelder proposed two alternative mechanistic pathways for formation of benzo[b]thiophene. Pathway A, favored by Venuto et al. (14), involves anti-Markovnikov 1,2-addition of hydrogen sulfide to the vinyl group to give the intermediate 2-phenylethanethiol (which would undergo subsequent dehydrocyclization to benzo[b]thiophene). Pathway B involves 1,4-addition of hydrogen sulfide to styrene, presumably to give a tautomer of 2-ethylbenzenethiol as an intermediate. The isolation of ethanethiol, diethyl sulfide, pyridine, and thiophene as byproducts in the reaction of 2-VPy with hydrogen sulfide (8) indicates that at reaction conditions 1,2-addition occurs in this system. Analogously, the formation of sulfide III from 4-VPy and hydrogen sulfide (7) implies the formation of 2-(4-pyridyl)-ethanethiol (II) by 1,2-addition, but casts doubt on the pertinence of II and III as intermediates on the route to 1. On the other hand, the facile dehydrocyclization of 4-ethylpyridine-3-thiol to 1 (albeit under somewhat different reaction conditions) (6) lends credence to a pathway of type B. The present studies were conducted in an effort to check further the possibilities of a pathway of type A for the conversion 4-VPy → 1. Exploratory runs (1-14, Table 1) were conducted at 630 ± 15°, in a flow system with hydrogen sulfide or nitrogen as carrier gas, and for relatively short apparent reaction times. Based on these results two additional series of runs (one under conditions conducive to thermolysis only, and the other under conditions conducive to heterogeneous catalysis) were also made (vide infra).

Runs 1-5 were made with 4-VPy as substrate but with variation in reactor packing used (glass helices, ferrous sulfide, chromia-alumina, stainless steel sponge). In each of these cases thienopyridine 1 was clearly identified as a reaction product. In runs 2-4 the yield of 1 was very small (1-2%) while the main product was sulfide III (60-68% yield). If one takes into account the fact that our data are

TABLE I

Exploratory Runs for the Formation of Thieno[2,3-c]pyridine (I) at 630° (a)

| | Starting Material | | | Percentage Yields (b) | | | | |
| | | Weight (g.) | Carrier Gas | | | | | |
Run No.	Formula			4-MePy	4-EtPy	4-VPy	I	Other
1	4-VPy (c)	50 (d)	H_2S	0	10	16	7	III,46 (e)
2-4	4-VPy (f)(g)	50	H_2S	3 (h)	14	15	2	III,60 (i)
6	4-PyCH$_2$CH$_2$SH(II)	64	H_2S	10	14	5	7	
7	II	24 (j)	N_2	15	1	43	5	Ph-Ph,3
8	(4-PyCH$_2$CH$_2$)$_2$S(III)	58	H_2S	7	13	11	12 (k)	
9	III	41	N_2	11	9	38	9 (k)	
10	4-PyCH$_2$CH$_2$SCH$_2$Ph(IV)	30	H_2S	5	9	5	11	$PhCH_3$,43 (ℓ)
11	IV	30	N_2	11	3	2	9	$PhCH_3$,8 (ℓ)
12	(4-PyCH$_2$CH$_2$)$_2$S$_2$(V)	12 (m)	H_2S	14	17	0	2 (n)	
13	4-PyCH$_2$CH$_2$\\S (VI) 2-PyCH$_2$CH$_2$⟋	30	H_2S	5	9	0	8 (k)	VII,8 (o)
14		30	N_2	6	0	5	5 (k)	VII,5 (o,p)

(a) Unless otherwise indicated, reactions were conducted in a steel tube (monel) packed with pyrex glass helices (3/32″ in diameter, the substrate was added neat at a rate of 15-20 drops/minute and the carrier gas was introduced at a standard rate of flow (cf. Experimental Section). (b) Except for runs 10 and 11 the method of processing the reaction mixture was such that components of b.p. <ca. 120° (760 mm.) would not be detected. Yields of 4-MePy are minimal values due to possible experimental losses through volatility. Other deviations in nitrogen balance for the reactions are caused by formation of non-distillable polymers and tars. (c) 4-VPy is 4-vinylpyridine. (d) Added at 30 drops/minute neat. (e) III is (4-PyCH$_2$CH$_2$)$_2$S. (f) Run 2 was made with a glass tube; run 3, with a glass tube packed with FeS; Run 4, with a monel tube packed with stainless steel sponge, rate of addition of 24 drops/minute. (g) Also used (35 g.) in run 5, with packing of Harshaw Chemical Co., Cr-0101T catalyst (1/8″ pellets), 12% Cr$_2$O$_3$-2% MgO-86% Al$_2$O$_3$. Run 5 gave 4% of I (only product for which an analysis was made). (h) Yields shown refer to run 4 and, except for III, are higher than in runs 2 and 3. (i) Range of yields. 60-68% of III for runs 2-4. (i) A solution of II in 200 ml. of benzene was added at 15-20 drops/minute. (k) Based on the stoichiometry of 1 (PyCH$_2$CH$_2$)$_2$S → 1 I. (ℓ) Other products: pyridine, trans-stilbene, and 2-phenylbenzo[b]-thiophene (cf. Experimental Section). (m) A solution of disulfide V in 25 ml. of benzene was added at a rate of 20-25 drops/minute. (n) Based on the stoichiometry 1 V → 2 I. (o) Other products: 2-MePy and 2-EtPy (cf. Experimental Section). VII is thieno[3,2-b]-pyridine. (p) Also 14% 2-VPy and 1% pyrrocoline (18).

based on vpc and nmr analyses, results of these three runs seem consistent with the observations of Hansch and Carpenter, who had less sophisticated methods of detection available and might easily have missed a small amount of I present. It was tentatively assumed, on the basis of the findings of Moore and Greensfelder (corroborated by recent studies of Venuto, Landis, and Boswell) for the styrene system, that the transformation 4-VPy → I would be heterogeneously catalyzed. However, under the conditions used in our runs, thermal processes alone suffice for interpretation of the results.

Runs 6-14 were made under the thermolytic conditions of run 1. Runs 6-7, 8-9, and 12 were used to check on the possibilities that thiol II, sulfide III, or disulfide V (respectively) might serve as intermediates in the reaction 4-VPy → I. From the yields of I found, it is apparent that II and III may be intermediates, but that V is an unlikely one. Benzyl 2-(4-pyridyl)ethyl sulfide (IV) was tried as a substrate (runs 10-11) since it is easily prepared (98% yield, by base catalyzed condensation of 4-VPy and benzyl mer-captan), is a stable liquid at room temperature (convenient for introduction into the reactor), and should undergo thermolysis preferentially at the PhCH$_2$—S bond (vide infra). In fact, the best yield of I per pyridyl moiety (ca. 10%) from these exploratory runs was obtained with substrate IV.

For preparative purposes the conversion IV → I was studied further (runs 15-19), as a function of reaction temperature, under conditions (Vycor tube, longer isothermal zone of packed glass helices, more careful temperature control, lower rate of carrier gas flow) designed to foster selective bond thermolysis. The percentage yield of I (from 4-VPy) rose from 39 at 580° to 58 at 605° (optimal temperature) and then fell to 15 at 645° (see Experimental). It is thus clear that the two-step synthesis 4-VPy → IV → I is the best available route to I. By-products were not determined in runs 15-19.

A third series of experiments (runs 20-22, Table II) was conducted with 4-VPy and hydrogen sulfide as reactants at temperatures below 630°, in order to check for possible

TABLE II

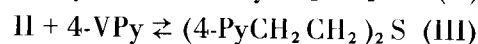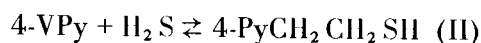Reaction of 4-VPy with H_2S in the Presence of
Chromia-Alumina (a)

Run No.	20	21	22
Reaction Temp.	420°	500°	550°
	Mole Percentage Yield		
4-MePy	29.6	31.7	46.9
4-EtPy	32.6	11.2	4.7
4-VPy	14.5	12.7	11.5
I	1.7	14.5	13.2
Unidentified (b)	(5.1)	(12.0)	(8.8)
Residue (c)	(15.7)	(17.5)	(19.8)

(a) Total quantities of 10.5 g. (0.1 mole) of 4-VPy and 0.4 mole of H_2S were added over a period of 80 minutes to a stainless steel tube (1.6 cm. i.d.) packed with 96 g. of fresh catalyst. See footnote (g), Table I. (b) Percentage by weight of total distilled product of b.p. $\leqslant 210°$ (1 mm.). (c) Percentage by weight of total product of b.p. $>210°$ (1 mm.).

occurrence of heterogeneous catalysis. At 500° and 550° the yield of I (ca. 14%) was again higher than in any exploratory run at 630°, but it was still considerably below that found for thermolysis of IV. Nonetheless, catalysis of the reaction is apparent since control experiments using glass helices as packing at 500° and 550° gave only traces of I. It is also noteworthy that yields of 4-MePy were much larger than those of 4-EtPy in runs 21 and 22, in contrast to findings for runs 1-4.

From the results of runs 1-9 it is presumed that 4-VPy, II, and III are interconvertible under reaction conditions (Scheme I). Since only minor amounts of II were

Scheme I

$$4\text{-VPy} + H_2S \rightleftarrows 4\text{-PyCH}_2\text{CH}_2\text{SH} \quad (\text{II})$$

$$II + 4\text{-VPy} \rightleftarrows (4\text{-PyCH}_2\text{CH}_2)_2 S \quad (\text{III})$$

detected in the effluent it is probable that II is a short-lived intermediate in the transformations which occur (15). In the absence of a stabilizing atmosphere of hydrogen sulfide one should expect reversion of II and III to 4-VPy to a considerable extent. This is noted in runs 7 and 9 (cf. runs 6 and 8, respectively) where the effluent contains ca. 40% of 4-VPy (cf. styrene system) (14). On the other hand, despite this reversion to 4-VPy, starting materials II and III also give 4-MePy, 4-EtPy, and I in higher combined yields in all runs than one finds in runs 1-4, and I is formed in comparable or better yields in these cases. Thus, both II and III qualify as plausible intermediates in the formation of these secondary products.

The steps in Scheme I may be visualized as occurring either by base-catalyzed or by free radical processes (or both). In the former case, the pyridine moiety itself would serve as the base to foster nucleophilic attack of HS^- and $4\text{-PyCH}_2\text{CH}_2S^-$ at the β-carbon of the vinyl group (15). Although the β-carbon is thus more electron-poor than the α-carbon, radical attack by $HS\cdot$ and $4\text{-PyCH}_2\text{CH}_2S\cdot$ should also occur there (anti-Markovnikov addition) (16,17a) because of formation of the resonance-stabilized entities, VIII and IX, respectively. It is conceivable that either type of initial mechanistic step could be facilitated by a

$$4\text{-Py}\overset{\bullet}{\text{C}}\text{HCH}_2\text{SH} \qquad 4\text{-Py}\overset{\bullet}{\text{C}}\text{HCH}_2\text{SCH}_2\text{CH}_2\text{Py-4}$$
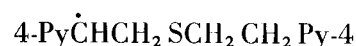
$$\text{VIII} \qquad\qquad\qquad \text{IX}$$

heterogeneous catalyst (19,20).

At 630° all bonds in starting molecules II-V (and VI, vide infra), except those involved in aromatic ring skeletal structures (21), should be susceptible to homolysis. It is thus possible to account qualitatively for all of the products isolated in runs 1-14 in terms of the formation and secondary reactions of free radical moieties (e.g. $4\text{-PyCH}_2\cdot$ → 4-MePy; $4\text{-PyCH}_2\text{CH}_2\cdot$ → 4-EtPy and 4-VPy; benzene → Ph· → biphenyl, in run 7). Compound I probably forms via $4\text{-PyCH}_2\text{CH}_2S\cdot$ (and/or $4\text{-PyCH=CHS}\cdot$, cf. proposal for the styrene-hydrogen sulfide system) (14).

The low yield of I from the disulfide V is consistent with previous indications that alkyl disulfides do not give preferential thermolysis of the S–S bond, but instead initially undergo a more facile non-radical molecular transformation (22). The absence of 4-VPy amongst the products of run 12 is somewhat surprising.

Results from runs 13 and 14 are qualitatively similar to those from runs 8 and 9, respectively. In addition, the nearly equal yields of the pairs of isomeric compounds, 2- and 4-MePy, 2- and 4-EtPy, and thienopyridines I and VII, respectively, are consistent with expectations as based on thermolytic processes and on the nearly equal strengths reported for the bonds 2-PyCH_2–H and 4-PyCH_2–H (23). The higher yield of 2-VPy (14%) than of 4-VPy (5%) in run 14, implies that 4-VPy may be more susceptible to secondary reactions than 2-VPy is.

Special characteristics of the product distribution in runs 10 and 11 are ascribed to preferential thermolysis of the $\text{PyCH}_2\text{CH}_2\text{S}–\text{CH}_2\text{Ph}$ bond, believed to be the weakest one in the molecule (24). The $4\text{-PyCH}_2\text{CH}_2\text{S}\cdot$ moiety then goes to I, while the benzyl radical leads to toluene (particularly in the presence of hydrogen sulfide), stilbene, and 2-phenylbenzo[b]thiophene (25).

As in the cases of thieno[2,3-b]pyridine and thieno-[3,2-b]pyridine (10), signals for all five protons of I are separately identifiable in the nmr spectrum and are correlatable with the structure of the compound on the basis of

analogy with the isoquinoline and benzo[b]thiophene systems. Long-range coupling between H-3 and H-7 is also apparent.

EXPERIMENTAL (27)

Preparation and Source of Starting Materials.

4-Vinylpyridine (4-VPy), obtained from Reilly Tar and Chemical Corp. (Indianapolis), was distilled just before use. 2-(4-Pyridyl)ethanethiol (II) was synthesized by the method of Bauer and Gardella (15) and stored as the hydrochloride until needed, whereupon it was regenerated with concentrated aqueous ammonia solution. The nmr spectrum of II (neat) showed broad singlets for SH (1H) and CH_2CH_2 (4H) at high field and a split doublet of doublets (J = 6 Hz) for the pyridyl protons (4H) in the aromatic region. Bis-2-(4-pyridyl)ethyl sulfide (III) was obtained as the crude combined distillation residues from runs 1-5 (vide infra); nmr (neat): singlet for CH_2CH_2 and split doublet of doublets (J = 6 Hz) for pyridyl protons. Bis-2-(4-pyridyl)ethyl disulfide (V) was synthesized essentially according to a reported procedure (15). 2-(2-Pyridyl)ethanethiol, prepared as per Bauer and Gardella (15), nmr (neat)-multiplets (in order of increasing δ) for SH and CH_2CH_2 at high field and for β-H, γ-H, and α-H in the aromatic region (relative areas, 1:4:2:1:1), was converted to a picrate, obtained as bright yellow prisms from ethanol, m.p. 100-101°, lit. (15) 89°.

Anal. Calcd. for $C_{13}H_{12}N_4O_7S$: C, 42.39; H, 3.29; N, 15.21; S, 8.70. Found: C, 42.38; H, 3.17; N, 15.19; S, 8.28.

2-(2-Pyridyl)ethyl 2-(4-Pyridyl)ethyl Sulfide (VI).

To an ice-cold, stirred solution of 40 g. (0.29 mole) of 2-(2-pyridyl)ethanethiol and sodium ethoxide (prepared from 0.75 g., 0.03 g.-atom, of sodium) in 80 ml. of absolute ethanol was added (over a period of 30 minutes) 30.2 g. (0.29 mole) of 4-VPy. The mixture was stirred at room temperature for 4 hours and then diluted with water. Most of the solvent was removed in vacuo and the residue was extracted with ether. Evaporation of the dried (sodium sulfate) ether layer left VI as a yellow liquid (quant. yield); nmr signals (carbon tetrachloride) at δ = 2.71 (s, 4, γ-CH_2CH_2), 2.93 (s, 4, α-CH_2CH_2), 6.8-7.2 (m, 4, β-H), 7.3-7.7 (m, 1, γ-H), and 8.3-8.6 ppm (m, 3, α-H).

The dipicrate formed a yellow powder from ethanol, m.p. 158.5-159.5°.

Anal. Calcd. for $C_{26}H_{22}N_8O_{14}S$: C, 44.45; H, 3.16; N, 15.95; S, 4.56. Found: C, 44.59; H, 3.34; N, 15.80; S, 4.98.

Benzyl 2-(4-Pyridyl)ethyl Sulfide (IV).

(a) From 4-Vinylpyridine.

The method was the same as that used for VI, except that 35 g. (0.28 mole) of α-toluenethiol (Distillation Products white label) was employed in place of 2-(2-pyridyl)ethanethiol and the total reaction time was 2.5 hours. Evaporation of solvent gave 63 g. (98%) of IV as a green liquid; nmr signals (carbon tetrachloride) at δ = 2.4-2.8 (m, 4, CH_2CH_2), 3.62 (s, 2, benzylic CH_2), 6.8-7.0 (overlapping d of doublets, 2, pyridyl β-H), 7.25 (s, 5, C_6H_5), and 8.2-8.5 (overlapping d of doublets, 2, pyridyl α-H).

The picrate was obtained as a canary yellow powder from ethanol, m.p. 112-113°.

Anal. Calcd. for $C_{20}H_{18}N_4O_7S$: C, 52.40. H, 3.96; N, 12.22; S, 6.99. Found: C, 52.63; H, 4.08; N, 12.37; S, 7.08.

(b) From 2-(4-Pyridyl)ethanethiol (II).

To an ice-cold, stirred solution of II (2 g., 0.014 mole) and sodium ethoxide (prepared from 0.5 g., 0.022 g.-atom, of sodium)

in absolute ethanol (35 ml.) was added dropwise 1.91 g. (0.015 mole) of benzyl chloride. The mixture was stirred at room temperature for 2 hours, filtered to remove sodium chloride, and evaporated to yield 2.5 g. (78%) of IV as a brown liquid, identical in nmr with product from (a).

Apparatus and General Procedure.

For runs 1-14 the reaction chamber consisted of a vertically mounted tube (either of pyrex glass, 2 cm. i.d.; or of monel steel, 2.6 cm. i.d.) packed to a depth of 24 cm. and heated by an external furnace to a temperature of 630° ± 15° (as sensed by a thermocouple placed between the reaction tube and the heating element). Tube packings, indicated in Table I, were pre-heated in situ at the reaction temperature for 1-2 hours in a stream of carrier gas, either hydrogen sulfide (Matheson, 99.5% minimum purity) or nitrogen (Industrial Air Products, 99.9% minimum purity). Gas flow (0.012 mole/minute for hydrogen sulfide, 500 ml./minute for nitrogen) was continued during the reaction proper while the substrate (either neat or in solution in reagent-grade benzene) was added at a rate of 15-20 drops/minute (unless otherwise noted) to the top of the reaction chamber. For 4-vinylpyridine (4-VPy) as substrate, a rate of addition of 16.6 drops/minute corresponds to a molar ratio of 4:1 for hydrogen sulfide:4-VPy. Other molar ratios were obtained by altering the dropping rate. Effluent from the reactor was collected in air- and ice-cooled traps. When addition of substrate was complete, heating and gas flow were discontinued.

In general, for each run, the cooled packing was removed from the reactor tube and extracted with three 200-ml. portions of boiling acetone. The extract, combined with contents of the traps, was filtered and saved for isolation of products.

Runs 15-19 were conducted in a vertically mounted Vycor tube (3 cm. i.d.) packed to a depth of 45 cm. with 3/32-inch Pyrex glass helices throughout an isothermal zone (estimated variation in temperature ± 3°) and with a flow rate of hydrogen sulfide of ca. 10 liters/hour. The neat liquid sulfide (50 g.) was added dropwise at a uniform rate over a period of 1.7 hours. The residue from evaporation of acetone washings of the cooled helices was combined with contents of the traps and dissolved in ether.

Runs 20-22 were made in a flow system described previously (28). The chromia-alumina packing, which formed a zone ca. 45 cm. long was activated at 450° in a stream of nitrogen for 1 hour, then at 500° in a stream of hydrogen sulfide (flow rate, 4 liters/hour) for 1 hour, and finally at the reaction temperature (hydrogen sulfide flow rate 7.5 liters/hour, maintained throughout the reaction) for 30-40 minutes. Following the reaction proper (80 minutes) the packing was washed in situ with 50 ml. of benzene, removed from the tube, and extracted with boiling methanol. Combined organic solutions were evaporated at 18 mm. and 25°. An acetone solution of the residue was filtered and re-evaporated.

Isolation and Identification of Products.

In runs 1-14 the solution of products in acetone was distilled in vacuo. A forerun (b.p..< 50°/20 mm.) was discarded. A low-boiling fraction (b.p. 50-150°/20 mm.) and a high-boiling fraction (b.p. 25-220°/1 mm.) were collected. The low-boiling fraction was first analyzed semi-quantitatively by vpc by means of a 0.25" x 5'-column of 15% Carbowax 20M on Chromosorb P at 150° and a He flow rate of 50 ml./minute. It was then analyzed more accurately by nmr with the help of a standard spectrum made from a synthetic mixture of 4-VPy, 4-MePy, 4-EtPy, acetone, and water. The high-boiling fraction was analyzed similarly except that (a) in vpc the 4-VPy peak observed was assumed to arise from thermal decomposition of sulfide III and (b) the standard nmr spectrum was obtained on a synthetic mixture of 4-VPy, III, thiol II, and

thienopyridine I. In runs 1-5 the distillation residue was a clear liquid which was identified as the sulfide III by nmr (comparison with that of an authentic sample), by picrate formation, m.p. 183-184°, lit. (7) 185-186°, and by its decomposition to 4-VPy and hydrogen sulfide on heating above 230° at 1 mm. In other runs, non-distillable residues were also obtained but (unless otherwise noted) they were not examined further. Combined high-boiling fractions from runs 6,8, and 9 were chromatographed on alumina with benzene as eluent to give I as a white semi-solid, identical with an authentic sample (5), as based on direct nmr spectrum as well as on m.p. and m.m.p. of the picrate.

In run 7 the high-boiling fraction was dissolved in benzene and extracted with excess 20% hydrochloric acid. The product from basification of the acidic extract was analyzed as before. The benzene layer was washed with water, dried, evaporated to a very small volume, and chromatographed on alumina (150 g.) with cyclohexane as eluent to give 4.6 g. (2.6% based on benzene used) of crude biphenyl, m.p. 65-68°, identified by direct comparison with an authentic sample.

In runs 10 and 11 the crude product mixture was first distilled at room pressure. The distillate, found (by nmr analysis) to contain mainly toluene plus a small amount of pyridine, was washed with 10% hydrochloric acid and then with water, dried, and examined by ir spectroscopy. Only toluene was present. An ether solution of the high-boiling fraction was washed in the same manner and evaporated to give trans-stilbene (4-5%), identified by m.p., m.m.p., and nmr spectrum with an authentic sample. The acetone-soluble portion of the non-distillable fraction was chromatographed on alumina (Alcoa F-20, 100 g.) with benzene as eluent. A crystalline fraction (m.p. 169.5-170.5°, from petroleum ether) was identified as 2-phenylbenzo[b]thiophene (ca. 8% in run 10, 13% in run 11) by direct comparison with an authentic sample prepared from 1,2-diphenylethane by the method of Horton (26).

In run 13 other products identified by nmr and vpc analyses were 2-MePy (5%) and 2-EtPy (7%); in run 14, 2-MePy (5%), 2-EtPy (3%), 2-VPy (14%), and pyrrocoline (1%) (18). The yields reported for I and VII are adjusted for differences in vpc detector responses of these compounds as based on a standard mixture.

In runs 15-19 ether solutions of the crude products were extracted with 10% hydrochloric acid. Basification of the acid solution and distillation of the ether extract thereof gave I, b.p. 73-75° (0.5 mm.), converted largely to crystals on cooling, m.p. 59-60° on recrystallization from hexane, identical in vpc retention volume with an authentic sample purified by sublimation, lit. (5) m.p. 54-55°. Yields of I obtained were 39% at 580°, 58% at 605°, 30% at 620°, 24% at 635°, and 15% at 645°.

Residues from runs 20-22 were distilled in vacuo. The total distillate up to 210° (1 mm.) was analyzed quantitatively by vpc on two different columns with temperature programming from 100-180°. Stationary phases consisted of 10% silicone gum rubber SE-30 on 60-80 mesh Chromosorb W (0.25" x 5') and 10% Carbowax 20M on 60-80 mesh Chromosorb P (0.37" x 5'). The products were also isolated by preparative vpc and compared directly with reference samples by ir spectra.

Nmr Spectrum of Thieno[2,3-c]pyridine (I).

The nmr spectrum of I (carbon tetrachloride) showed signals at $\delta = 7.22$ (d of doublets, 1, H-3; $J_{2,3} = 5.8$, $J_{3,7} = 0.9$ Hz), 7.57 (d of doublets, 1, H-4; $J_{4,5} = 5.7$, $J_{4,7} = 1.2$ Hz), 7.63 (d, 1, H-2), 8.44 (d, 1, H-5), and 9.12 (broadened pseudotriplet, 1, H-7). In analogy with isoquinoline (29) the signal at lowest field is ascribed to the lone proton (H-7) which is α to the heterocyclic N-atom, while the next signal is ascribed to the proton (H-5) which is α to

the N-atom on the other side. Coupling between H-5 and H-7 was not observed (cf. pyridine derivatives $J_{2,6} = 0$-0.6) (9, 30). Consistent with observations for the methylbenzo[b]thiophenes (31). as well as the thieno[2,3-b]pyridine and thieno[3,2-b]pyridine systems (10), the signal for H-2 (a simple doublet) is found at lower field than that of H-3. Correlation of the two doublets of doublets at higher fields with H-3 and H-4 is less certain (due to broadening in the H-7 signal) but is based on expectations that $\delta_4 > \delta_3$ and that the long-range coupling constant $J_{3,7} < 1$ (10).

Acknowledgment.

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(1) This investigation was supported by Research Grant No. CA-5969 from the National Cancer Institute, U. S. Public Health Service. For Paper VI, see reference 9.

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