Condensed Thiophenes from Sulfur Bridging. II. Catalyzed Reaction of Azabiaryls with Hydrogen Sulfide (1)

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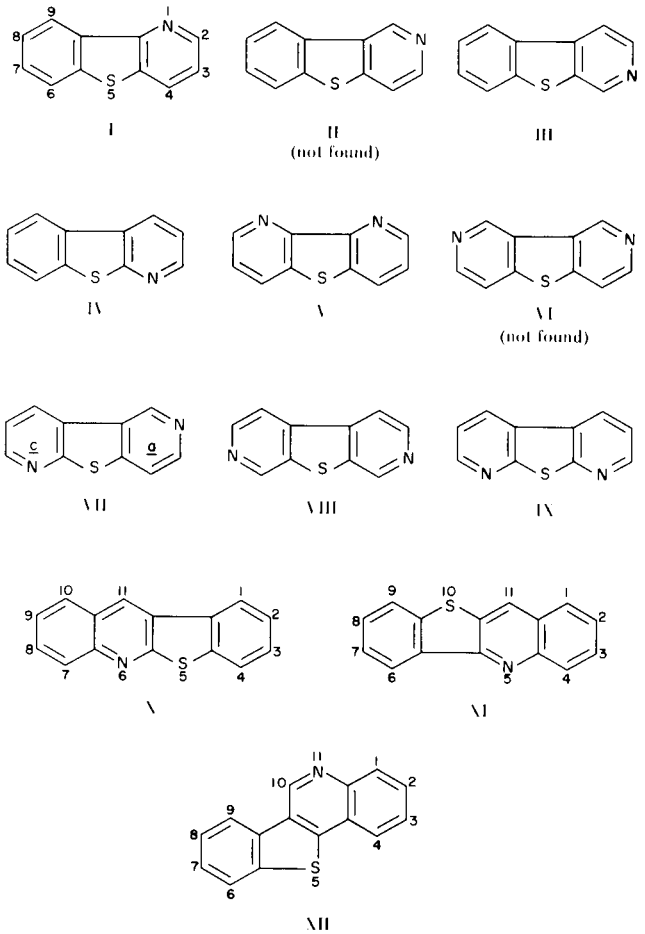
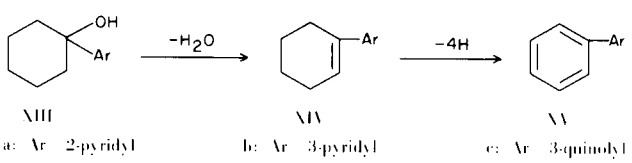
Received February 19, 1971

Sulfur bridging into the phenylpyridines, 2- and 3-phenylquinolines, and the symmetric bipyridines was effected by means of hydrogen sulfide and an alumina catalyst at 630° to give [1]benzothienopyridines, [1]benzothienoquinolines, and thienodipyridines, respectively. Structures of products were assigned on the bases of spectral and chromatographic studies, as well as of separate syntheses. Relative yields of the various products are rationalized in terms of a model for interaction between a chemisorbed sulfur atom and the substrate molecule.

In a preceding paper (3) we reported the conversion of biphenyl into dibenzothiophene and of phenanthrene into phenanthro[4,5-*bcd*]thiophene by means of hydrogen sulfide and a chromia-alumina-magnesia catalyst (Harshaw Cr-0101T) in a flow system at 630°. The present paper describes the extension of this procedure to use of the three phenylpyridines, the three symmetrical bipyridines, and 2- and 3-phenylquinolines as substrates. From analogy with the biphenyl case one would expect to obtain from these various substrates the four possible [1]benzothienopyridines (I-IV), five (V-IX) of the ten possible thienodipyridines, and three (X-XII) of the ten possible catenated [1]benzothienoquinolines (4). In fact, ten of these compounds were isolated from the reactions (Table I), while II and VI were neither separated from the reaction products nor clearly identified therein. It is presumed that the general methodology could be used to effect sulfur bridging in a wide variety of other biaryl, azabiaryl, and angularly catenated polycyclic aromatic substrates.



The substrates 2-phenylpyridine (2-PhPy), 3-phenylpyridine (3-PhPy), and 3-phenylquinoline (3-PhQ) were prepared by dehydration-dehydrogenation of the corresponding 1-azaryl-1-cyclohexanols (XIII). For 3-PhPy, the carbinol XIIIb (5) was converted directly into XVb under the same catalytic conditions as used in the sulfur-bridging



reaction, except that nitrogen (inert) was employed as a carrier gas in place of hydrogen sulfide. For syntheses of 2-PhPy and 3-PhQ the dehydration step to XIV was carried

TABLE I

Sulfur Bridging Reactions with Hydrogen Sulfide at 630° (a)

Run No.	Substrate (A) Formula	Weight (g.)	Benzene Solvent (ml.)	Packed Reactor Vol. (cc.)	Molar Ratio H_2S/A	Product(s) Formed	Yield (%) (b)	Recovered A (%)	Analytical Method Used
1	2-PhPy	37.2	0	75	6	I	11	85	vpc
2-4	I + 2-PhPy	(c)	0	75	6	I	10-15		vpc (d)
5	I + 2-PhPy	(e)	0	75	6	I	22		vpc (d)
6	2-PhPy (f)	39	0	75	6	I	1	87	vpc (d)
7	2-PhPy	13.8	52	156	20	I	35	53	pmr (g)
8	XIIIa	29.3	40	75	8	I	10	79	vpc
9	XIVa	40	0	75	6	I	7	87	vpc (d)
10	3-PhPy	7	27	150	20	IV	25	8	vpc
11	XIIIb	10	90	156	56	IV	18	2	vpc (h)
12	4-PhPy	13.8	52	150	20	III	1.6	39	isol.
13	2-PhQ	11	30	156	20	XI	18		isol.
14	2-PhQ	50	200	156	19	XI	3.7	66	isol.
15	2-PhQ (i)	11	30	150	20		0	100	pmr
16	3-PhQ	12	52	150	20	X XII	12 5	7	isol.
17	2,2′-biPy (j)	10	50	75	40	V	8-11	54-71	pmr
18	2,2′-biPy	10	38	150	21	V	6	24	pmr
19	2,2′-biPy (k)	10	30	156	21		0	48	pmr
20	3,3′-biPy	18.5	70	156	21	IX VII	12 3.3	15	pmr
21	4,4′-biPy (l)	10	57-70	150	20	VIII	1-3	13-20	pmr

(a) Except in runs 2-4, 6, 15, and 19 the reactor was packed with fresh Harshaw Cr-0101T catalyst. Either the neat liquid substrate or a benzene solution of the substrate was added to the reactor at a rate of 15-30 drops/minute. (b) Yield is based on total moles of substrate charged to the reactor. (c) The total product from run 1 was recycled through the same batch of catalyst three more times and analyzed after each cycle. (d) Analyses by pmr gave results within 1-2% of those found by vpc. (e) The total product from run 4 was recycled through a fresh batch of catalyst. (f) Tube packing was Houdry HA-100 pure alumina. (g) Isolation gave yields of 29% of I and 44% of recovered 2-PhPy. (h) The same yields were obtained on isolation. (i) Tube packing was glass helices. (j) For six identical runs. (k) Tube packing was Harshaw Al-0104T pure alumina. (l) For three similar runs.

out first (as a batchwise process) and dehydrogenation was then effected in the catalytic reactor. In fact, with hydrogen sulfide as the carrier gas carbinols XIIIa and XIIIb, as well as alkene XIVa (6), were converted directly into the same [1]benzothienopyridines as formed from their phenylpyridine congeners (runs 8, 9, 11).

Observation of the data in Table I shows that the sulfur-bridging reaction of these azabiaryls is heterogeneously catalyzed, in the same general way as occurs for biphenyl (3,7). Thus, under otherwise identical conditions 2-PhQ gave no reaction (run 15) when the reactor tube was packed with glass helices, but it formed an 18% yield of XI (run 13) when chromia-alumina-magnesia packing was used instead. Likewise, use of pure alumina with 2-PhPy (run 6) and 2,2′-biPy (run 19) gave little or no sulfur bridging, in contrast to the effect of chromia-alumina-magnesia (runs 1 and 18, respectively). With biphenyl as substrate (3) pure alumina was approximately 0.6 times as effective as the mixed oxide catalyst.

Structures of products formed were checked by microanalyses, ultraviolet spectra (8), and pmr spectra (*vide infra*). In most cases additional confirmatory evidence for the proposed structure was also provided. Barring molecular rearrangement, only one sulfur-bridged product is possible from each of the substrates 2-PhPy, 4-PhPy, 2-PhQ, 2,2′-biPy, and 4,4′-biPy. The structure of I (from 2-PhPy) was confirmed by separate synthesis, which involved treatment of the salt of 3-aminobenzo[*b*]thiophene with malondi-

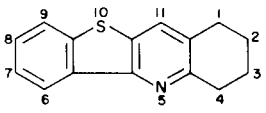
TABLE II

Proton Magnetic Resonance Data for Some Condensed Thienopyridines (a)

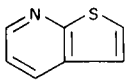
Compound No.	Chemical Shift, in δ (b) H_α	H_β	H_γ or ($H_{\alpha'}$)	Coupling Constant, in Hz (c) $J_{\alpha,\beta}$	$J_{\beta,\gamma}$	$J_{\alpha,\gamma}$ or ($J_{\alpha',\beta}$)	Other Signals; Remarks
I	8.66	7.17	7.99	4.5	8.0	1.5	7.4-7.9 (m, H-6 to H-8), 8.3-8.6 (m, H-9)
III	8.60	?	(9.11)	5.4		(<1)	7.2-8.3 (m, H_β plus H-6 to H-9)
IV	8.57	7.25	8.21	4.7	8.0	1.6	7.1-7.6 (m, H_β, H-7, H-8), 7.6-8.1 (m, H-6, H-9)
V	8.83	7.34	8.10	4.9	8.9	1.5	
VII	?	7.76	(9.32)	5.0		(<1)	For *a* ring. H_α signal, obscured; $H_{\alpha'}$ signal, broad.
VII	8.67	7.40	8.41	4.6	8.0	1.5	For *c* ring.
VIII	8.76	8.08	(9.28)	5.6		(*ca.* 1)	
IX	8.79	7.50	8.42	4.7	8.0	1.7	
X			8.51				7.2-8.2 (m, H-1 to H-4, H-7 to H-10)
XI			8.51				7.1-8.0 (m, H-1 to H-3, H-7 to H-9), 8.1-8.4 (m, H-4), 8.55-8.8 (m, H-6)
XII	9.43						7.2-8.3 (m, H-1 to H-4, H-6 to H-9)
XVI			7.61				1.4-2.2 (m, 2 H-2, 2 H-3), 2.6-3.3 (m, 2 H-1, 2 H-4), 7.1-7.9 (m, H-7 to H-9 plus H_γ), 8.3-8.7 (m, H-6)

(a) Solvent used, deuteriochloroform. (b) α, α′, β, and γ refer to positions with respect to the nitrogen atom in a pyrido ring. See Figure 1 for the symbolism used. Parenthesized values refer to $H_{\alpha'}$. (c) Parenthesized values refer to $J_{\alpha',\beta}$. $J_{\alpha,\alpha'} \cong 0$.

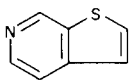
aldehyde tetraethyl acetal (MDTA) in the general manner previously described (9). Compounds III (from 4-PhPy) and XI (from 2-PhQ) agreed in physical properties with products previously reported by others (10,11). In addition, XI was synthesized independently by treatment of the salt of 3-aminobenzo[*b*]thiophene with 2-hydroxymethylenecyclohexanone and dehydrogenation of the intermediate XVI. Compound V is isosteric (12) with



XVI



XVII



XVIII

1,10-phenanthroline. Analogously V shows high retentivity in tlc on alumina (13) and dissolves readily in aqueous ferrous sulfate to give a colored complex (14). In contrast, VII and IX (derived from 3,3′-biPy) show lower retentivities on alumina and are insoluble in aqueous ferrous sulfate. The ultraviolet spectrum of IX (the major product from 3,3′-biPy) shows little change on going from neutral to acidic ethanolic solution--in contrast to the observation of appreciable change for the spectrum of VII. Comparison with ultraviolet spectral and pK_a data for thieno[2,3-*b*]pyridine (XVII) and thieno[2,3-*c*]pyridine (XVIII) (8) corroborates the structural assignment of IX and indicates that VII should be one of the other two possible isomers (VI and VII) derivable from the substrate used. The single product obtained from reaction of 3-PhPy was assigned structure IV since (a) it differed in physical properties from those reported for the known alternative product II (10,15), and (b) it was also obtainable by reaction of MDTA on the salt of 2-aminobenzo[*b*]-thiophene (16). Structures of compounds X and XII (derived from 3-PhQ) were corroborated by the facts that (a) the former was more readily eluted from a mixture of the two compounds adsorbed on alumina (13), (b) differences in ultraviolet spectral changes analogous to those of IX and VII, respectively, were observed, and (c) the singlet in the pmr spectrum for the one proton on the pyridine ring occurred further downfield in XII (α proton) than in X (γ proton).

In the phenylpyridine and bipyridine series the 2- and 2,2′-isomers gave higher yields of products than the 4- and 4,4′-isomers, respectively. None of the yields from the

azabiaryls was as large as that from biphenyl (59% under comparable conditions) (3). For 3-PhPy as substrate (run 10) only one product, IV, which arises from bridging into the α position of the pyridine ring, was found. Bridging into the γ position to give II did not occur to a detectable extent. With 3-PhQ, on the other hand, bridging into both α and γ positions took place (run 16), though the ratio (X/XII) of isomeric products was > 2:1 in favor of α-bridging. For 3,3'-biPy (run 20) the relationship of yields IX:VII:VI of 3.6:1:~0 again reflects a strong preference for α-bridging over γ-bridging. This preference cannot be ascribed solely to differences in reactivities of α, β, and γ positions *per se*; for then 2-PhPy and 4-PhPy might be expected to give comparable yields of products (from β-bridging in each case) and some II should have been detected. Failure to detect any thiobiarenols (or sulfides and disulfides derived from two molecules of substrate) would indicate that the 1,4-cycloaddition of sulfur is effected during a single period of adsorption. Desorption then would occur only when formation of the aromatized sulfur-bridged product or its dihydro derivative is complete.

Tentatively, we propose that (a) both the substrate molecule and the reactant sulfur species are adsorbed on the catalyst surface during the transition state of the reaction and (b) the relative yield of product obtained can be rationalized largely in terms of the relative geometric facility of forming the requisite transition complex. For phenanthrene and biphenyl it is assumed that the substrate molecule is adsorbed flatwise (or nearly flatwise, π-type adsorption) onto the catalyst surface [as proposed in chromatography on alumina (17-21)] so that close proximity of the chemisorbed sulfur (which projects outward from the catalyst surface) to the 1,4-system of the substrate permits cycloaddition to occur fairly readily. The azabiaryls, on the other hand, may be adsorbed either flatwise or edgewise (through the non-bonding electrons, *n*-type adsorption) (13,19,20,22-25). For edgewise adsorption (presumably preferred for 3-PhPy and 3,3'-biPy) sulfur bridging should be geometrically facile at an α position to the nitrogen atom (of the *n*-adsorbed ring) and geometrically prohibited at a γ position. For 4-PhPy and 4,4'-biPy edgewise adsorption should be strongly preferred, but only flatwise adsorption could give sulfur bridging. Flatwise adsorption may be preferred in 2-PhPy and 2-PhQ due to steric hindrance to edgewise adsorption. In 3-PhQ one may have appreciable adsorption in both manners. For 2,2'-biPy, edgewise adsorption (by chelation to a single surface site) (26) should be preferred, but reaction ought to occur more readily on singly anchored molecules.

Pmr spectral data for the sulfur bridged products are presented in Table II. Greek letters used refer to positions on the pyrido rings, as indicated in Figure 1. As noted for

Figure 1

quinoline, isoquinoline (27a), and the six isomeric thienopyridines (9,28-31) the signal for $H_{\alpha'}$ falls at lower field ($\delta > 9.1$ in deuteriochloroform) than for H_{α} (range 8.0-8.9), except for the high value of H_{α} = 9.43 in XII. Signals for H_{α} in XII and $H_{\alpha'}$ in VII fall especially far downfield because these protons occupy angular positions (27b,32) in phene-type structures. The relationship of $J_{\alpha,\gamma} > J_{\alpha',\beta}$ has likewise been noted in the benzo and thienopyridines (9,27c,28-30). In I, XI, and XVI angular protons (H-9, H-6, and H-6, respectively) show long range shielding by the non-bonding electron pair of the nitrogen atom (27d,32).

EXPERIMENTAL (33)

Preparation and Source of Starting Materials.

4-Phenylpyridine, 2,2'-bipyridine, and 4,4'-bipyridine were obtained from commercial sources. 4,7-Phenanthroline (34) was oxidized and decarboxylated by the method of Smith (35) to form 3,3'-bipyridine, purified by chromatography with alumina and benzene; pmr (neat) δ (relative values) 6.57 (d of doublets, 2H, $J_{4,5}$ = 8 Hz, $J_{5,6}$ = 4.8 Hz, H-5 and H-5'), 7.12 (d of overlapping doublets, H-4 and H-4'), 7.95 (d of doublets, 2H, $J_{4,6}$ = 1.8 Hz, H-6 and H-6'), 8.24 ppm (d, 2H, $J_{2,4}$ = 2.2 Hz, H-2 and H-2'). 1-(2-Pyridyl)-1-cyclohexanol (XIIIa) [m.p. 43-44°, lit. (6) 42-43°] and 1-(2-pyridyl)-1-cyclohexene (XIVa) [b.p. 93-94° (1 mm.); pmr (carbon tetrachloride) δ 1.3-2.6 (m, 8H, methylene protons), 6.5-7.5 (m, 4H, H-3 to H-5 plus vinylic proton), 8.4-8.6 ppm (m, 1H, H-6); lit. (6) b.p. 97-98° (3 mm.)] were prepared by the method of Lochte, *et al.* (6). 1-(3-Pyridyl)-1-cyclohexanol (XIIIb), m.p. 88-90° (73%), was prepared from 3-bromopyridine, *n*-butyllithium, and cyclohexanone in the same manner as used for carbinol XIIIc (*vide infra*).

A portion of about 20 g. of 2-phenylquinoline-4-carboxylic acid (Aldrich) was mixed intimately with 2.3 g. of copper powder (purified, J. T. Baker) in a sublimation apparatus. The mixture was heated at 200° (20 mm.) to effect decarboxylation plus evaporative distillation of the resultant 2-phenylquinoline, m.p. 82.5-83.5°, picrate m.p. 188.5-190.5°; lit. (36) 82-83.5°, 191-192°. The process was interrupted periodically to remove product and to replenish the supply of carboxylic acid (total of 126 g. used, yield 74%) in contact with the catalyst.

1-(3-Quinolyl)-1-cyclohexanol (XIIIc).

To 125 ml. of 1.6 *M* solution of *n*-butyllithium (0.2 mole) in hexane at -70° was added 50 ml. of ether and then (dropwise, with stirring in an atmosphere of nitrogen) a solution of 20.8 g. (0.1 mole) of 3-bromoquinoline (freshly distilled) in 50 ml. of ether. After 45 minutes more, a solution of 20 g. (0.2 mole) of cyclohexanone in 50 ml. of ether was added dropwise over a period of 40 minutes. The mixture was stirred at -70° for 2 hours, warmed to room temperature, and poured on ice. The hydrolysis mixture was acidified with hydrochloric acid, washed with ether, and

basified with sodium hydroxide. Extraction with ether gave 13.8 g. (61%) of crude product, obtained as needles on crystallization from acetone, m.p. 152-153°; pmr (deuteriochloroform) δ 1.0-2.2 (m, 10H, methylene protons), 3.83 (s, 1H, OH), 7.2-8.3 (m, 5H, H-4 to H-8), 8.89 ppm (d, 1H, $J_{2,4}$ = 2 Hz, H-2).

Anal. Calcd. for $C_{15}H_{17}NO$: C, 79.3; H, 7.5; N, 6.2. Found: C, 79.3; H, 7.4; N, 6.0.

1-(3-Quinolyl)-1-cyclohexene (XIVc).

An intimate mixture of 10 g. of preceding carbinol XIIIc and 10 g. of potassium bisulfate was heated at 190° (20 mm.) for 3 hours until water was no longer evolved. The cooled residue was dissolved in water. The solution was basified with sodium hydroxide and extracted with carbon tetrachloride to give white crystals from pentane, yield 6.9 g. (75%), m.p. 46.5-47.5°; pmr (carbon tetrachloride) δ 1.4-2.6 (m, 10H, methylene protons), 6.0-6.3 (m, 1H, vinylic proton), 7.1-8.2 (m, 5H, H-4 to H-8), 8.89 ppm (d, 1H, $J_{2,4}$ = 2 Hz, H-2).

The picrate was obtained as canary yellow needles from ethanol, m.p. 219-220°.

Anal. Calcd. for $C_{21}H_{18}N_4O_7$: C, 57.5; H, 4.1; N, 12.8. Found: C, 57.5; H, 4.1; N, 12.7.

Catalytic Apparatus and General Observations.

The flow apparatus for conducting heterogeneously catalyzed reactions was described previously (37). Conditions for the individual sulfur bridging runs are indicated in Table I. Although benzene (used as solvent in some cases) is not completely inert under the reaction conditions, the biphenyl and dibenzothiophene formed in small amounts therefrom are readily separable from the desired condensed thienopyridine products and appear to offer no deleterious effects on the main reaction.

In general, fresh catalyst and substrate were used in each run. Such was the case in run 1, where an 11% yield of I was formed. Repetitive cycling of the total product from run 1 through the used catalyst (runs 2-4), but with fresh carrier gas, gave no appreciable change in composition of the effluent. Hence, it appears that the catalyst was almost totally deactivated during run 1 and that I is neither formed nor decomposed thermally at 630°. The alternative possibility that a virtual steady state is attained amongst the reactants and products (during runs 2-4) was disproved by run 5, wherein the total product from run 4 was passed through fresh catalyst. A marked increase in the percentage composition of I in the effluent was again noted. Comparative yields in runs 13 and 14 are likewise ascribed to catalyst deactivation. Thus, the total weight of XI formed in each of these runs was nearly the same despite the large difference in amounts of 2-PhQ substrate used.

The optimum molar ratio of hydrogen sulfide to substrate was not clearly established. Comparison of runs 17 and 18 shows that there is little improvement in yield upon increasing this ratio above 20:1. Examination of the data in runs 1, 5, and 7, moreover, leads to the implication that (if effects of catalyst deactivation are taken into account) a ratio of 6:1 may suffice. For correlation of product yield with structure of substrate (independent of aspects of catalyst deactivation and of ratio of carrier gas to substrate), it seems reasonable to use yield data directly from runs 7, 12, 13, 16, 18, and 21. Observed yields in runs 10 (comparatively high) and 20 (comparatively low) would need to be adjusted (say to 18-20% each for IV and IX and to 5-6% for VII) before comparison.

Analytical Procedures.

Analyses of crude product mixtures from the catalytic reactor were performed by vpc with an F & M Model 810 dual column chromatograph, a stationary phase of Carbowax 20M, and a thermal conductivity detector. Peaks were identified by comparison of retention times with those of authentic samples. Correlation of measured area with weight of each product was made by noting the change in area of a specific peak on adding a weighed amount of the corresponding compound to a weighed sample of the crude product.

A Varian Associates A-60 nmr spectrometer was used to determine spectra of purified samples, as well as to analyze crude reaction mixtures. In run 7, for example, the ratio of pmr integrated areas in the regions δ 8.4-8.7 (H_α in 2-PhPy plus H_α and H_γ in I) and δ 6.7-8.2 (8 other protons in 2-PhPy plus H_β and H-6 to H-9 in I) was used to ascertain the mole fractions of 2-PhPy and I in the crude product. The method was checked with a synthetic standard mixture.

The analytical method used in each run is indicated in Table I. Unless otherwise noted, column chromatography was conducted with Alcoa F-20 alumina as adsorbent plus cyclohexane (used first to remove sulfur, biphenyl, dibenzothiophene, and cracking products) and then benzene as eluents.

Catalytic Dehydrogenation and Dehydration Reactions.

Addition of the neat alkene XIVa (41.8 g.) (rate of 16 drops/minute) in nitrogen carrier gas (flow rate, 580 ml./minute) to the catalytic reactor gave dehydrogenation to 2-phenylpyridine (2-PhPy), isolated by distillation, b.p. 89-90° (1 mm.); yield, 29.7 g. (73%). Similarly, alkene XIVc (38 g., in benzene as solvent) gave (at 600°) 24.5 g. (66%) of 3-phenylquinoline (3-PhQ), isolated by chromatography, recrystallized from pentane, m.p. 51.5-52.5°, picrate m.p. 206-207°; lit. (38) 52° and 205°, respectively. Also carbinol XIIIb (25.3 g. in benzene) formed 3-phenylpyridine (3-PhPy), crude yield 12.4 g. (56%), purified further by chromatography and distillation, b.p. 105-110° (0.5 mm.).

The picrate of 3-PhPy formed canary yellow needles from ethanol, m.p. 168-170°; lit. (39) 158-160°, 162-163°.

Anal. Calcd. for $C_{17}H_{12}N_4O_7$: C, 53.1; H, 3.2; N, 14.6. Found: C, 53.1; H, 3.2; N, 14.7.

[1]Benzothieno[3,2-*b*]pyridine (I).

A. From 2-Phenylpyridine.

The product from run 7 was distilled up to 180° (20 mm.) to remove 2-PhPy. The residue crystallized from pentane to give 4.8 g. (29%) of I, m.p. 76-80°, obtained as prisms (m.p. 81-82°) on recrystallization from benzene-petroleum ether (30-60°) plus sublimation *in vacuo*.

Anal. Calcd. for $C_{11}H_7NS$: C, 71.3; H, 3.8; N, 7.6; S, 17.3. Found: C, 71.4; H, 4.1; N, 7.3; S, 17.1.

B. From 3-Nitrobenzo[*b*]thiophene.

To a vigorously stirred solution of 20 g. (0.09 mole) of stannous chloride dihydrate in 20 ml. of concentrated hydrochloric acid and 10 ml. of ethanol in an atmosphere of nitrogen was added 2 g. (0.011 mole) of 3-nitrobenzo[*b*]thiophene (40) at such rate as to maintain a reaction temperature of 30-40°. The reaction mixture was then held at 50° for one hour, heated to 80°, and treated with a solution of 2.2 g. (0.013 mole) of malondialdehyde tetraethyl acetal (Aldrich) and 0.5 g. of anhydrous zinc chloride in 10 ml. of ethanol. After 3 hours at 80°, the mixture (dark in color) was poured into water, basified with 40% aqueous sodium hydroxide solution, and extracted with carbon tetrachloride. The black tar which remained on evaporation of the solvent was chromatographed on Brinkman neutral alumina (40 g.) with cyclohexane and benzene as eluents to give 0.6 g. (29%) of I, m.p. 80-81°, identical with product from A as based on mixture melting point, as well as on pmr and vpc analyses.

The picrate formed yellow prisms from ethanol, m.p. 211-212°.

Anal. Calcd. for $C_{17}H_{10}N_4O_7S$: C, 49.3; H, 2.4; N, 13.5; S, 7.7. Found: C, 49.1; H, 2.5; N, 13.6; S, 7.9.

[1]Benzothieno[2,3-*c*]pyridine (III).

The product from run 12 was distilled at 0.3 mm. pressure to remove most of the 4-PhPy (5.4 g. recovered). The residue was chromatographed to give more 4-PhPy and then a mixture of III and 4-PhPy. Crystallization of the latter fraction from petroleum ether (30-60°) gave pure III (0.27 g., 1.6%), m.p. 97-98.5°, picrate m.p. 253.5-254.5°; lit. (10) 96-98° and 256°, respectively.

[1]Benzothieno[2,3-*b*]pyridine (IV).

A. From 1-(3-Pyridyl)-1-cyclohexanol (XIIIb).

The product from run 11 was chromatographed to yield 1.8 g. (18%) of crude IV. Crystallization from pentane and sublimation at 20 mm. pressure gave a powder, m.p. 75-75.5°.

Anal. Calcd. for $C_{11}H_7NS$: C, 71.3; H, 3.8; N, 7.6; S, 17.3. Found: C, 71.1; H, 3.9; N, 7.8; S, 17.1.

The picrate formed canary yellow prisms from ethanol, m.p. 188.5-189°.

Anal. Calcd. for $C_{17}H_{10}N_4O_7S$: C, 49.3; H, 2.4; S, 7.7. Found: C, 49.6; H, 2.6; S, 7.6.

B. From Bis-(2-benzo[*b*]thienyl)ammonium Hexachlorostannate (XIX).

To a warm (60°), stirred solution of 5 g. (7.9 mmoles) of XIX (16), 4.5 g. of anhydrous ferric chloride, and 0.1 g. of anhydrous zinc chloride in 10 ml. of ethanol in an atmosphere of nitrogen was added (over a period of 20 minutes) a solution of 1.8 g. (8.2 mmoles) of malondialdehyde tetraethyl acetal in 5 ml. of absolute ethanol. The temperature of the mixture was raised to 80° for 1.5 hours. The mixture was poured into ice and concentrated hydrochloric acid, basified, and extracted with ether. The liquid residue from evaporation of the extract was chromatographed (benzene eluent) to give crystalline IV, identical with product from A as based on pmr analysis. The picrate (m.p. 188-188.5°; yield 0.06 g., 2% from XIX) showed no depression of melting point on admixture with picrate from A.

Thieno[3,2-*b*:4,5-*b'*]dipyridine (V).

The product from run 17 was extracted repeatedly with hot petroleum ether (30-60°) to remove 2,2'-biPy and the residue was chromatographed (benzene-chloroform eluent) to give prisms of V (2-5%), m.p. 148.5-149° after recrystallization from carbon tetrachloride and sublimation *in vacuo*.

Anal. Calcd. for $C_{10}H_6N_2S$: C, 64.5; H, 3.3; N, 15.0; S, 17.2. Found: C, 64.7; H, 3.4; N, 15.0; S, 17.1.

The methiodide formed bright yellow needles from ethanol-ether, m.p. 207-207.5°.

Anal. Calcd. for $C_{11}H_9IN_2S$: C, 40.3; H, 2.8; I, 38.7; N, 8.5; S, 9.8. Found: C, 40.2; H, 2.8; I, 38.7; N, 8.4; S, 9.7.

Compound V dissolved in 0.001 *M* aqueous ferrous chloride to give a bright yellow complex; uv max 425 nm.

Thieno[2,3-*b*:5,4-*b'*]dipyridine (IX).

The product from run 20 was chromatographed to give (with benzene and more polar eluents) a mixture of 3,3'-biPy, VII, and IX. Further chromatography with cyclohexane gave mixtures of 3,3'-biPy plus IX (eluted first) and of 3,3'-biPy plus VII (*vide infra*). The former mixture was recrystallized from ethanol to give crude IX (1.5 g., 7%), purified further by fractional sublimation at 130° (0.3 mm.) and additional recrystallizations, obtained as fluffy needles, m.p. 169-169.5°.

Anal. Calcd. for $C_{10}H_6N_2S$: C, 64.5; H, 3.3; N, 15.0; S, 17.2. Found: C, 64.7; H, 3.4; N, 14.9; S, 16.8.

The methiodide formed amber prisms from ethanol, m.p. 241° dec.

Anal. Calcd. for $C_{11}H_9IN_2S$: C, 40.3; H, 2.8; N, 8.5. Found: C, 40.1; H, 3.0; N, 8.5.

Thieno[2,3-*b*:4,5-*c'*]dipyridine (VII).

The aforementioned mixture of 3,3'-biPy plus VII from run 20 was recrystallized from ethanol to give crude VII (0.67 g., 3%), purified further as for IX, obtained as needles, m.p. 137.5-138°.

Anal. Calcd. for $C_{10}H_6N_2S$: C, 64.5; H, 3.3; S, 17.2. Found: C, 64.7; H, 3.1; S, 17.2.

Thieno[2,3-*c*:5,4-*c'*]dipyridine (VIII).

The product from run 21 was purified by chromatography. Elution with benzene gave recovered 4,4'-biPy and then with chloroform gave a mixture of 4,4'-biPy and VIII. Crystallization of the mixture from ethanol gave crude VIII (117 mg., 1%), recrystallization from ethanol-petroleum ether (30-60°), obtained as needles, m.p. 177-178°.

The methiodide formed amber needles from methanol, m.p. *ca.* 300° dec.

Anal. Calcd. for $C_{11}H_9IN_2S$: C, 40.3; H, 2.8; I, 38.7; N, 8.5; S, 9.8. Found: C, 40.3; H, 2.9; I, 38.5; N, 8.5; S, 9.5.

[1]Benzothieno[3,2-*b*]quinoline (XI).

A. From 2-Phenylquinoline.

The product from run 13 was recrystallized from ethanol to give 2.1 g. (18%) of needles, m.p. 171.5-172.5°, lit. (11) 172°.

Anal. Calcd. for $C_{15}H_9NS$: C, 76.6; H, 3.9; N, 5.9. Found: C, 76.4; H, 3.9; N, 5.7.

B. *Via* 1,2,3,4-Tetrahydro[1]benzothieno[3,2-*b*]quinoline (XVI).

As in the synthesis of I (Part B), 34.8 g. (0.195 mole) of 3-nitrobenzo[*b*]thiophene was reduced with stannous chloride. The reduction mixture was heated to reflux and treated with 18 g. of anhydrous zinc chloride and 42 g. (0.33 mole) of 2-hydroxymethylenecyclohexanone (41). The mixture was refluxed for 2 hours longer and then processed in the foregoing manner. Chromatography gave crude XVI (4%), obtained as faintly yellow prisms (m.p. 106-107°) on recrystallization from hexane-ethanol.

Anal. Calcd. for $C_{15}H_{13}NS$: C, 75.3; H, 5.5; N, 5.8; S, 13.4. Found: C, 75.6; H, 5.5; N, 5.8; S, 13.1.

A mixture of 0.25 g. (1 mmole) of XVI and 0.46 g. (2 mmoles) of 2,3-dichloro-5,6-dicyanobenzoquinone in 14 ml. of benzene was refluxed in an atmosphere of nitrogen for 2.3 hours. The mixture was cooled, diluted with hexane, and filtered. The residue from evaporation of the filtrate was chromatographed with alumina and benzene to give crude XI, sublimed at 0.5 mm. pressure (yield 31 mg., 13%, m.p. 155-160°), and then recrystallized from ethanol m.p. 169-169.5°, identical with a sample from part A as based on mixture melting point, pmr, and ir spectra.

[1]Benzothieno[2,3-*b*]quinoline (X).

The product from run 16 was distilled up to 220° (20 mm.) and the residue was crystallized from cyclohexane. Chromatography of the mother liquors gave recovered 3-PhQ (0.9 g., 7%), while chromatography of the crystalline mixture yielded crude X (1.65 g., 12%, m.p. 140-141°, eluted with cyclohexane-benzene) and then crude XII (0.65 g., 5%, m.p. 155-160°, eluted with benzene), *vide infra*. Recrystallization of X from ethanol produced faintly cream-colored needles, m.p. 142-142.5°.

Anal. Calcd. for $C_{15}H_9NS$: C, 76.6; H, 3.9; N, 5.9; S, 13.6. Found: C, 76.5; H, 3.9; N, 5.9; S, 13.6.

[1]Benzothieno[3,2-*c*]quinoline (XII).

Recrystallization of foregoing crude XII from ethanol plus sublimation of 130° (0.5 mm.) gave white prisms, m.p. 175.5-176°.

Anal. Calcd. for $C_{15}H_9NS$: C, 76.6; H, 3.9; N, 5.9; S, 13.6. Found: C, 76.7; H, 3.6; N, 5.9; S, 13.5.

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