The Chemistry of Pyridine. IX. Deoxydative Substitution of Pyridine *N*-Oxides by Thiophenols in the Presence of Sulfonyl Halides[1]

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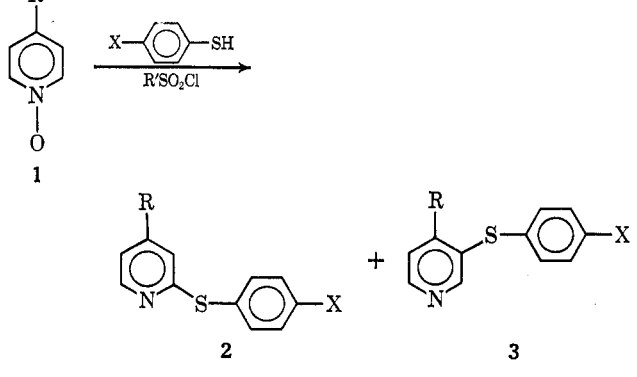
A number of pyridine and quinoline 1-oxides were substituted by thiophenols in the presence of sulfonyl chlorides in either benzene or chloroform to produce α- and β-arylthiopyridines in 30–70% yield. A considerable amount of β substitution (40–60% of total) was observed. When 2,6-lutidine 1-oxide was treated with thiophenol and benzenesulfonyl chloride in chloroform, 3- and 4-arylthio-2,6-lutidine were obtained in a ratio of 4:1. 2,4,6-Collidine 1-oxide was substituted by thiophenol to yield 3-phenylthio-2,4,6-collidine. All of the reactions are postulated to proceed *via* 1-sulfonyloxy-2-arylthio-1,2-dihydropyridine intermediates with the exception of 2,6-lutidine 1-oxide, where either a 1,2- or 1,4-dihydropyridine can be involved.

It was established that pyridine and quinoline *N*-oxides are ring substituted by mercaptans in the presence of various acid halides and anhydrides to form a mixture of 2- and 3-pyridyl and -quinolyl sulfides.[3–5] The substitution pattern and other evidence suggested that α and β substitution arose from a common 1-acyloxy-2-alkylthio-1,2-dihydropyridine intermediate.[5] Although simple mercaptans readily participated in ring substitutions when hot acetic anhydride was utilized both as acylating agent and solvent,[5] ethyl thioglycolate and thiophenols did not react. Since these thiols were acetylated quantitatively under these conditions, it appeared that their rate of attack on the activated heteroaromatic ring was too slow to compete with acylation. The electron-attracting nature of the ester in ethyl thioglycolate and that of the arene in thiophenols could decrease the nucleophilicity of these thiol groups sufficiently to contribute to this subtle difference in behavior.

To promote nucleophilic attack by these thiols on the ring, its electrophilicity would have to be enhanced. In changing the acylating agent from acetic anhydride to a sulfonyl halide, deoxydative substitution of **1** took place to form a mixture of sulfides **2** and **3** (Table I).



The reaction is attributed to attack by the thiophenol on the highly electrophilic α position of **4** to form **5**. The facile departure of sulfonate ion from **5** to form the highly energetic nitrenium–carbonium ion pair, **6**, is in concert with the ready N–O cleavage experienced by oxime, hydroxamic acid, and *O*-hydroxylamine sulfonates.[6–8] The subsequent involvement of **7** to form **3** has been discussed previously.[5] Support for the ion pair in a tight solvent cage, **6**, in these reactions emerges from the fact that, in changing from benzene to chloroform, the isomer ratio for a particular reaction remains constant (Table I).

TABLE I[a]

R in **1**	X in thiophenol	R′ in sulfonyl halide	Solvent[b]	Yield, %	Isomer distribution[c] **2**	**3**	Disulfide[f] ArSSAr
H	H	CH_3	B	27.2	40	60[d]	60.2
H	H	C_6H_5	B	30.2	41	59[d]	52.8
H	H	C_6H_5	C	45.7	39	61[d]	
H	Cl	C_6H_5	C	50.0	37	63[e]	35.6
H	*tert*-C_4H_9	C_6H_5	B	33.0	32	68	30.9
H	*tert*-C_4H_9	C_6H_5	C	36.1	38	62	
CH_3	H	CH_3	B	41.0	56	44	37.4
CH_3	H	CH_3	C	62.3	54	46	19.8
CH_3	H	C_6H_5	B	33.6	67	33	51.1
CH_3	H	C_6H_5	C	72.3	66	34	21.8
CH_3	Cl	CH_3	B	49.2	46	54	27.4
CH_3	Cl	C_6H_5	C	73.2	44	56	19.3
CH_3	*tert*-C_4H_9	C_6H_5	B	40.4	38	62	43.0
CH_3	*tert*-C_4H_9	CH_3	C	55.5	27	73	
CH_3	*tert*-C_4H_9	C_6H_5	C	53.6	34	66	27.4
tert-C_4H_9	H	C_6H_5	C	25.0	57	43	
tert-C_4H_9	Cl	C_6H_5	C	26.6	49	51	
tert-C_4H_9	*tert*-C_4H_9	C_6H_5	B	34.8	37	63	60.2
tert-C_4H_9	*tert*-C_4H_9	C_6H_5	C	28.9	40	60	58.7

[a] The reactions were carried out under the following standard set of conditions: 1 equiv of the sulfonyl halide was added to a stirred equimolar mixture of the *N*-oxide and thiol in either benzene or chloroform at 0°. [b] B = benzene, C = chloroform. [c] Isomer distribution determined by pmr, except where noted. [d] Determined by gc. [e] Determined by column chromatography. [f] Not determined where space is blank.

Additional evidence for the high level of induced electrophilicity at the β position of **6** is provided from several experiments. A bulky group at the γ position offered little hindrance, since 4-*tert*-butylpyridine 1-oxide experienced a high degree of β substitution (Table I). 2,6-Lutidine 1-oxide was not ring substituted by mercaptans in acetic anhydride[5] but reacted with thiophenol and benzenesulfonyl chloride to give a mixture of 3- and 4-arylthio-2,6-lutidine in the ratio of better

(1) Taken in part from the Ph.D. dissertation of K. F. King, University of Illinois at the Medical Center, Chicago, Ill. Presented at the 160th National Meeting of the American Chemical Society, Chicago, Ill., Sept 1970.

(2) National Science Foundation Trainee, 1966–1970.

(3) L. Bauer and T. Dickerhofe, *J. Org. Chem.*, **29**, 2183 (1964); *ibid.*, **31**, 939 (1966).

(4) L. Bauer and A. L. Hirsch, *ibid.*, **31**, 1210 (1966).

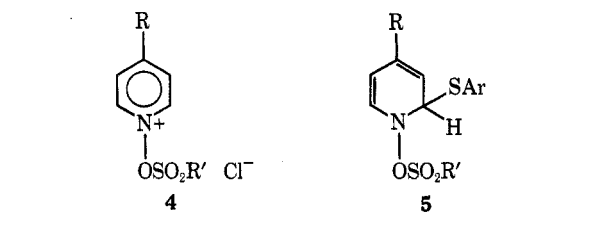
(5) F. M. Hershenson and L. Bauer, *ibid.*, **34**, 655, 660 (1969).

(6) L. G. Donaruma and W. Z. Heldt [*Org. React.*, **11**, 1 (1960)] report that the rate of rearrangement was proportional to the strength of the esterifying acid, *i.e.*, $C_6H_5SO_3H > RCO_2H$.

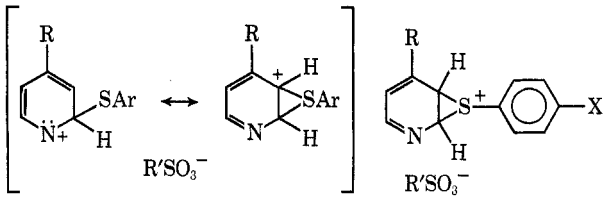
(7) The ease by which *O*-sulfonyl hydroxamates rearrange has been demonstrated frequently; see F. M. Hershenson, L. Bauer, and K. F. King, *J. Org. Chem.*, **33**, 253 (1968).

(8) J. P. Fleury, J. M. Biehler, and M. Desbois, *Tetrahedron Lett.*, 4091 (1969).

than 4:1. It is not surprising that the *N*-sulfonyloxy group imparted considerable electorphilic character to the γ position which provided the 4-arylthio-2,3-lutidine. An unanswered question is whether the β-substituted product is the result of sulfide migration from a 1,2- or 1,4-dihydropyridine derivative from 2,6-lutidine 1-oxide. The methyl group in the 2 position should not be able to prevent attack by thiophenol to form an intermediate analogous to **5**. Better support for attack on a carbon bearing a methyl group is advanced when it was discovered that 2,4,6-collidine 1-oxide was substituted by thiophenol in the presence of benzenesulfonyl chloride to furnish 3-phenylthio-2,4-collidine.



4 **5**



6 **7**

Change in Solvent.—Since solutions could not be maintained during each of the reactions in benzene or chloroform, few conclusions can be drawn beyond the one stated above regarding isomer distribution.

Change in Sulfonyl Halide.—These experiments indicate that a change from benzenesulfonyl to methanesulfonyl chloride resulted in a higher proportion of **3**, using similar substrates and solvents. Two effects operating in the same direction in **5** when R = CH_3 could be responsible for the relative increase of β substitution. The benzenesulfonyl derivative **5** (R = C_6H_5) imparts greater acidity to the α proton which is expected to be lost during the aromatization process. The more facile departure of benzenesulfonate to methanesulfonate ion, combined with the more acidic H-2, would favor α substitution. By the same token, scission of the methanesulfonate ion might be assisted by simultaneous migration of the sulfide in **5** to form **7** and thereby indirectly increase β substitution.

γ Substituent in 1.—Remarkable little variation was observed in β substitution as H was replaced by CH_3 and *tert*-C_4H_9, in comparable situations, which reinforces the proposed mechanism.

Para Substituent in the Thiophenol.—Although the data offer certain trends, these are interpreted with caution. For the reactions of pyridine 1-oxide with benzenesulfonyl chloride in chloroform, there appeared little change in the isomer distribution as the para substituent in the thiophenol was varied from H to Cl to *tert*-C_4H_9. Since no steric hindrance would be encountered at the γ position of pyridine 1-oxide, this would reflect few electronic effects due to the para substituent in the intermediate **7**. However, in reactions of both 4-picoline and 4-*tert*-butylpyridine 1-oxides, the percent of β isomer increased as the thiophenol X varied: *tert*-C_4H_9 > Cl > H. This could indicate that stabilization of **7** by the *tert*-butyl and chloro substituent aids its formation and leads to **3**, in the face of some steric encumberance at the γ position.

Related Reactions.—The reaction of lepidine 1-oxide with thiophenol and methanesulfonyl chloride gave a mixture of 2- and 3-phenylthiolepidines in the ratio of better than 4:1. The lesser amount of β substitution experienced in lepidine, compared to 4-picoline 1-oxide, is attributed to the inhibition of forming the equivalent structure to **7**, since in lepidine the benzenoid aromaticity would have to be disrupted.

When *tert*-butyl mercaptan was used as the thiol with 4-picoline 1-oxide and benzenesulfonyl chloride in chloroform, a poor yield of sulfides was obtained; the ratio of α to β substitution was 47:53. When these figures are compared with a ratio of 70:30 using acetic anhydride as the acylating agent,[5] they would point again to an increased electrophilicity at the β position when sulfonyl halides are employed. By contrast, ethyl thioglycolate produced only the 2-substituted sulfide. Apparently, migration was sufficiently discouraged by the lesser nucleophilicity of the sulfur nucleophile.

By-products.—In all of these reactions, the formation of a large amount of disulfides was quite apparent, but even more puzzling was the formation of a considerable quantity of the pyridine or quinoline related to the starting *N*-oxide; although no attempt was made to isolate pyridine or 4-picoline, the less water-soluble bases, like 4-*tert*-butylpyridine and lepidine, appeared as part of the distillate.[3] It seems plausible that the reduction of the *N*-oxide, and disulfide formation (at least, in part), can be linked to at least one process. Recent papers on the oxidation of thiols to disulfides by chloramine and the reactions of sulfenimides [$(RCO)_2NSR$] with thiols to form disulfides[9] suggests that sulfenamides could serve as precursors to disulfides. Such a sulfenamide could be created in our work if the sulfonate ion in **4** is displaced by ArSH to create the intermediate, R_3NSAr^+ Cl^-, and 1 mol of the sulfonic acid. A second attack by ArSH would then yield the disulfide and the pyridine (R_3N). At least this mechanism could explain the reduction of the *N*-oxide by the thiol and sulfonyl halide. It is realized, of course, that the pyridine-catalyzed reaction of thiophenol with sulfonyl halides yields disulfides directly.[10]

Experimental Section[11]

Starting Materials.—Generous gifts of the following chemicals are gratefully acknowledged: *tert*-butyl mercaptan from Pennwalt Chemical Co. and Phillips Petroleum Co.; 4-*tert*-butylpyridine, pyridine 1-oxide, 4-picoline 1-oxide, and 2,6-lutidine 1-oxides from Reilly Tar and Chemical Co. Alumina used was either Alcoa (grade F-20) or Woelm neutral (activity grade I)

(9) H. H. Sisler, N. K. Kotia, and R. E. Highsmith, *J. Org. Chem.*, **35**, 1742 (1970); K. S. Boustany and A. B. Sullivan, *Tetrahedron Lett.*, 3547 (1970); D. N. Harpp, *et al.*, *ibid.*, 3551 (1970).

(10) T. F. Parsons, J. D. Buckman, D. E. Pearson, and L. Field, *J. Org. Chem.*, **30**, 1923 (1965).

(11) Melting and boiling points are uncorrected. Nitrogen analyses were obtained by one of us (K. F. K.) using a Coleman nitrogen analyzer, Model 29. Pmr spectra were taken at 60 MHz using a Varian A-60 spectrometer. Signals are reported in parts per million (δ) downfield from internal tetramethylsilane (TMS). Each A-60 spectrum was calibrated by a sample of TMS (δ 0.0 in $CHCl_3$ (δ 7.28). Proton assignments were based on correct integral information, on chemical shifts anticipated fo the particular protons, and, whenever possible, spin–spin coupling constants (J) derived from first-order analysis. Only pertient pmr parameters are reported. All compounds gave appropriate parent ions in their mass spectra at 70 eV using a Hitachi Perkin-Elmer RMU-6D mass spectrometer equipped with a Honeywell Visicorder.

activated at 120° for 15 hr. Benzene was thiophene free and petroleum ether was the fraction of bp 30–60°. Thin layer chromatographs (tlc) were determined on silica gel with a fluorescent indicator (Eastman chromagram sheet 6060) using benzene–chloroform (1:1) as the developer. The spots were detected by uv light or iodine stains.

Gas chromatography (gc) was performed using a Varian Aero-Prep 700. Two columns were used. For the arylthiopyridines a diethylene glycol succinate column (5%) on Chromosorb G was used isothermally (180°). All other separations were effected utilizing SE-30 on Chromosorb W (20%) with the injection temperature reported and a power regulator setting of "50." Although determination of isomer ratios on the 5% DEGS column was not always possible because of broad peaks, a fraction often eluting over a period of 0.5 hr yielded pure samples for analytical purposes.

General Procedure B. Reaction of Pyridine 1-Oxide and Thiophenol with Benzenesulfonyl Chloride in Benzene.—To a vigorously stirred solution of pyridine 1-oxide (9.5 g, 0.1 mol) in benzene (100 ml) and thiophenol (11.02 g, 0.1 mol) in an ice water bath (4°) was added benzenesulfonyl chloride (17.66 g, 0.1 mol) in one portion. The temperature rose sharply to 31° and a fine precipitate appeared. The mixture was stirred in the ice bath for 0.5 hr and then washed with 5% NaOH (two 50-ml portions). The basic phase was back-extracted with benzene (two 30-ml portions) and the aqueous phase was not examined further. The combined benzene fractions were extracted with dilute HCl (1:3, three 50-ml portions). The acid extract was made basic (pH 10) with 50% NaOH and extracted with chloroform (three 50-ml portions). Distillation afforded 5.67 g, bp 107–109° (0.14 Torr). By means of gc the following compounds were collected (injection temperature 180°). **3-Phenylthiopyridine** [59%, retention time(rt) 121.2 min]: pmr ($CDCl_3$) δ 8.71 (H-2), 8.57 (H-6), 7.68 (H-4), 7.23 (H-5) ($J_{2,4} = J_{2,5} = 0.9$, $J_{4,5} = 7.9$, $J_{5,6} = 4.5$ Hz). *Anal.* Calcd for $C_{11}H_9NS$: N, 7.48. Found: N, 7.39. **2-Phenylthiopyridine** (41%, rt 140.6 min): pmr ($CDCl_3$) δ 8.55 (H-6), 7.35–7.80 (m, H-4 and phenyl protons), 6.86–7.20 (m, H-3, H-5) ($J_{3,6} = 1.1$, $J_{4,6} = 2.1$, $J_{5,6} = 4.5$ Hz). *Anal.* Calcd for $C_{11}H_9NS$: N, 7.48. Found: N, 7.54. This sulfide was described previously [lit.[12] bp 160–162° (8 Torr)].

Fom the benzene solution above was isolated phenyl disulfide (5.76 g, 52.8%), mp 54–56° (lit.[13] mp 60°). All other reactions performed in benzene were carried out similarly and the yields and isomer distribution recorded in Table I.

General Procedure C. With Benzenesulfonyl Chloride in Chloroform.—The reaction was carried out on the same scale as described for procedure B with chloroform (100 ml) as solvent. A minor modification in the work-up was essential since some arylthiopyridine hydrochlorides possessed appreciable solubility in chloroform and could not be extracted with dilute hydrochloric acid. After 0.5 hr, the mixture was extracted with 5% NaOH and the chloroform removed *in vacuo* and replaced by benzene (100 ml). The products were isolated as under procedure B and the results listed in Table I.

Reaction of Pyridine 1-Oxide and *p*-Chlorothiophenol.—The arylthiopyridines were distilled, bp 135–137° (0.15 Torr), and separated on alumina. **2-*p*-Chlorophenylthiopyridine**[14] (R_f 0.48) was eluted by petroleum ether: pmr ($CDCl_3$) δ 8.50 (H-6) ($J_{3,6} = 1.3$, $J_{4,6} = 1.9$, $J_{5,6} = 4.6$ Hz). *Anal.* Calcd for $C_{11}H_8ClNS$: N, 6.32. Found: N, 6.37. **3-*p*-Chlorophenylthiopyridine** (R_f 0.32) was eluted by benzene: pmr ($CDCl_3$) δ 8.81 (H-2), 8.71 (H-6) ($J_{2,4} = 2.4$, $J_{2,5} = 0.9$, $J_{4,6} = 1.7$, $J_{5,6} = 4.1$ Hz). *Anal.* Calcd for $C_{11}H_8ClNS$: N, 6.32. Found: N, 6.25.

p-Chlorophenyl disulfide was recrystallized from 95% ethanol, mp 68–70° (lit.[15] mp 72–74°).

Reaction of Pyridine 1-Oxide and *p-tert*-Butylthiophenol.—The sulfides were collected, bp 145–147° (0.10 Torr), and separated by gc (injection temperature 180°). **3-*p-tert*-Butylphenylthiopyridine** (rt 232.0 min): pmr ($CDCl_3$) δ 8.63 (H-2), 8.55 (H-6), 1.31 (*tert*-C_4H_9) ($J_{2,4} = 2.2$, $J_{2,5} = 0.8$, $J_{4,6} = 1.8$, $J_{5,6} = 4.8$ Hz). *Anal.* Calcd for $C_{15}H_{17}NS$: N, 5.76. Found: N, 5.68. **2-*p-tert*-Butylphenylthiopyridine** (rt 272.5 min): pmr ($CDCl_3$) δ 8.55 (H-6), 1.33 (*tert*-C_4H_9) ($J_{3,6} = 1.1$, $J_{4,6} = 1.9$, $J_{5,6} = 4.7$ Hz). *Anal.* Calcd for $C_{15}H_{17}NS$: N, 5.76. Found: N, 5.68.

The isomer distribution was checked by estimating the ratio of the *tert*-butyl signals (at 50-Hz sweep width). Because the peaks are singlets with no coupling and because of their close chemical shifts, peak height rather than integrated area was determined to be most accurate.

The original basic aqueous solution was extracted continuously (18 hr) with CH_2Cl_2. Distillation yielded pyridine 1-oxide 3.47 g, bp 104–105° (0.05 Torr), identified by its ir.

p-tert-Butylphenyl disulfide was recrystallized from 95% ethanol, mp 84–86° (lit.[16] mp 88.5–89°).

Reaction of 4-Picoline 1-Oxide and Thiophenol.—The arylthiopyridines boiled between 114 and 116° (0.15 Torr) and were separated by gc (injection temperature 180°). **3-Phenylthio-4-picoline** (rt 114.4 min): pmr ($CDCl_3$) δ 8.62 (H-2), 8.52 (H-6), 2.37 (CH_3) ($J_{5,6} = 4.8$ Hz). *Anal.* Calcd for $C_{12}H_{11}NS$: N, 6.96. Found: N, 6.85. **2-Phenylthio-4-picoline**[17] (rt 155.3 min): pmr ($CDCl_3$) δ 8.42 (H-6), 2.21 (CH_3) ($J_{3,6} = 0.8$, $J_{5,6} = 4.8$ Hz). *Anal.* Calcd for $C_{12}H_{11}NS$: N, 6.96. Found: N, 6.82.

The isomer distribution was checked by integration of the methyl signals at δ 2.37 and 2.21.

Reaction of 4-Picoline 1-Oxide and *p*-Chlorothiophenol.—The arylthiopyridines were collected, bp 124–126° (0.15 Torr), and separated on alumina. **2-*p*-Chlorophenylthio-4-picoline** was eluted by benzene (R_f 0.38): pmr ($CDCl_3$) δ 8.42 (H-6), 6.94 (H-5), 6.90 (H-3), 2.24 (CH_3) ($J_{3,6} = 1.1$, $J_{5,6} = 4.4$ Hz). *Anal.* Calcd for $C_{12}H_{10}ClNS$: N, 5.94. Found: N, 5.83. **3-*p*-Chlorophenylthio-4-picoline** (R_f 0.22) was eluted in later fractions by benzene: pmr ($CDCl_3$) δ 8.62 (H-2), 8.54 (H-6), 2.34 (CH_3) ($J_{5,6} = 5.1$ Hz). *Anal.* Calcd for $C_{12}H_{10}ClNS$: N, 5.94. Found: N, 5.90.

Reaction of 4-Picoline 1-Oxide and *p-tert*-Butylthiophenol.—The sulfides were distilled, bp 160–162° (0.2 Torr), and separated on alumina. **2-*p-tert*-Butylphenylthio-4-picoline** (R_f 0.25) was eluted by petroleum ether–benzene (1:1): pmr ($CDCl_3$) δ 8.31 (H-6), 6.82 (H-3), 6.34 (H-5), 2.16 (CH_3), 1.31 (*tert*-C_4H_9); (C_6D_6) 8.26 (H-6), 7.47 (4-Ar H), 6.83 (H-3), 6.34 (H-5), 1.62 (CH_3), 1.14 (*tert*-C_4H_9) ($J_{3,5} = 1.4$, $J_{3,6} = 0.8$ $J_{5,6} = 4.9$, $J_{5,CH_3} = 0.8$, $J_{3,CH_3} = 0.8$ Hz). A large shift (0.54 ppm) of the picoline methyl signal was observed when C_6D_6 was the solvent. A change to this solvent aided the determination of the isomer ratio. *Anal.* Calcd for $C_{16}H_{19}NS$: N, 5.44. Found: N, 5.50. **3-*p-tert*-Butylphenylthio-4-picoline** (R_f 0.145) was eluted with benzene: pmr ($CDCl_3$) δ 8.48 (H-2), 8.42 (H-6), 7.15 (H-5), 2.33 (CH_3), 1.27 (*tert*-C_4H_9); pmr (C_6D_6) 8.79 (H-2), 8.42 (H-6), 7.15 (4-Ar H), 6.64 (H-5), 2.08 (CH_3), 1.10 (*tert*-C_4H_9) ($J_{2,5} = 0.9$, $J_{5,6} = 4.8$, $J_{5,CH_3} = 0.6$ Hz). *Anal.* Calcd for $C_{16}H_{19}NS$: N, 5.44. Found: N, 5.38.

The aqueous basic layer from a reaction with benzenesulfonyl chloride in benzene was extracted (24 hr) with CH_2Cl_2. Solvents were removed and the residue chromatographed on alumina. Elution with $CHCl_3$ furnished 4-picoline 1-oxide (4.36 g, mp 180–183°).

Reaction of 4-*tert*-Butylpyridine 1-Oxide and Thiophenol.—Distillation of the products using benzenesulfonyl chloride in chloroform yielded 4-*tert*-butylpyridine (0.22 g, 3.26%, ir identical with that of the authentic sample) and a mixture of the arylthiopyridines and 4-*tert*-butylpyridine 1-oxide [6.07 g, bp 126–128° (0.14 Torr)]. The 4-*tert*-butylpyridine 1-oxide in the mixture was identified by tlc comparison with an authentic sample and its pmr [δ 1.33 (*tert*-C_4H_9), 8.28 (H-2, H-6)]. The mixture was separated on alumina. **2-Phenylthio-4-*tert*-butylpyridine** (R_f 0.52) was eluted by petroleum ether–benzene (1:1): pmr ($CDCl_3$) δ 8.51 (H-6), 1.16 (*tert*-C_4H_9) ($J_{3,6} = 2.1$, $J_{5,6} = 4.0$ Hz). *Anal.* Calcd for $C_{15}H_{17}NS$: N, 5.76. Found: N, 5.68. **3-Phenylthio-4-*tert*-butylpyridine** (R_f 0.36) was eluted by ether: pmr ($CDCl_3$) δ 8.55 (H-2), 8.50 (H-6), 1.50 (*tert*-C_4H_9) ($J_{5,6} = 5.4$ Hz). *Anal.* Calcd for $C_{15}H_{17}NS$: N, 5.76. Found: N, 5.82.

Isomer distribution and yield was determined by pmr. The peaks at δ 1.16 and 1.50 (*tert*-butyl signals) provided the isomer distribution and the one at δ 1.33 gave an estimate of the amount of 4-*tert*-butylpyridine 1-oxide.

(12) L. G. S. Brooker, *et al.*, *J. Amer. Chem. Soc.*, **73**, 5326 (1951).

(13) F. Scardiglia and J. D. Roberts, *Tetrahedron*, **3**, 197 (1958).

(14) C. K. Bradsher, L. D. Quin, R. E. LeBleu, and J. W. McDonald [*J. Org. Chem.*, **26**, 4944 (1961)] report bp 185–190° (10 Torr).

(15) H. R. Al-Kazimi, D. S. Tarbell, and D. Plant, *J. Amer. Chem. Soc.*, **77**, 2479 (1955).

(16) H. J. Backer and E. Westerhuis, *Recl. Trav. Chim. Pays-Bas*, **71**, 1071 (1952).

(17) L. Bauer and L. A. Gardella [*J. Org. Chem.*, **28**, 1323 (1963)] report bp 125° (0.3 Torr).

Reaction of 4-*tert*-Butylpyridine 1-Oxide and *p*-Chlorothiophenol.—Distillation of the basic fraction yielded 4-*tert*-butylpyridine [bp 44–46° (0.15 Torr)] and a mixture of the arylthiopyridines and 4-*tert*-butylpyridine 1-oxide [bp 149–151° (0.15 Torr)].

2-*p*-Chlorophenylthio-4-*tert*-butylpyridine (R_f 0.53) was eluted from alumina by petroleum ether–benzene (1:1): pmr ($CDCl_3$) δ 8.52 (H-6), 1.23 (*tert*-C_4H_9) ($J_{3,6}$ = 1.6, $J_{5,6}$ = 4.8 Hz). *Anal.* Calcd for $C_{15}H_{16}ClNS$: N, 5.04. Found: N, 4.98. **3-*p*-Chlorophenylthio-4-*tert*-butylpyridine** (R_f 0.35) was eluted by ether: pmr ($CDCl_3$) δ 8.63 (H-6), 8.59 (H-2), 1.50 (*tert*-C_4H_9) ($J_{5,6}$ = 4.4 Hz). *Anal.* Calcd for $C_{15}H_{16}ClNS$: N, 5.04. Found: N, 5.02.

Reaction of 4-*tert*-Butylpyridine 1-Oxide and *p*-*tert*-Butylthiophenol with Benzenesulfonyl Chloride (Method B).—A modification was required in the work-up since the sulfides could not be extracted from the benzene layer by 1:3 HCl. The benzene solution contained the sulfides and *p*-*tert*-butylphenyl disulfide in the ratio of 60.9 to 39.1 (pmr). Separation was achieved most satisfactorily on alumina. Petroleum ether eluted the disulfide, followed by **2-*p*-*tert*-butylphenylthio-4-*tert*-butylpyridine**, which was eluted by petroleum ether–benzene (1:1): bp 175–180° (0.2 Torr); pmr ($CDCl_3$) δ 8.40 (H-6), 7.52 (4-phenyl H), 7.00 (H-3 and H-5), 1.33 (pyridyl *tert*-C_4H_9), 1.17 (phenyl *tert*-C_4H_9); pmr (C_6D_6) δ 8.25 (H-6), 7.47 (4 phenyl H), 7.07 (H-3), 6.70 (H-5), 1.18 (pyridyl *tert*-C_4H_9), 0.98 (phenyl *tert*-C_4H_9) ($J_{3,5}$ = 1.8, $J_{3,6}$ = 0.7, $J_{5,6}$ = 5.1 Hz). *Anal.* Calcd for $C_{19}H_{25}NS$: N, 4.68. Found: N, 4.61.

3-*p*-*tert*-Butylphenylthio-4-*tert*-butylpyridine was eluted with ether: bp 175–180° (0.2 Torr); pmr ($CDCl_3$) δ 8.47 (H-2), 8.40 (H-6), 7.30 (H-5), 1.52 (pyridyl *tert*-C_4H_f), 1.27 (phenyl *tert*-C_4H_9); pmr (C_6D_6) δ 8.80 (H-2), 8.43 (H-6), 7.04 (H-5), 1.41 (pyridyl *tert*-C_4H_9), 1.14 (phenyl *tert*-C_4H_9) ($J_{5,6}$ = 5.1 Hz). *Anal.* Calcd for $C_{19}H_{25}NS$: N, 4.68. Found: N, 4.69.

Reaction of 3,5-Lutidine 1-Oxide and *p*-*tert*-Butylthiophenol with Benzenesulfonyl Chloride (Method C).—Distillation of the basic fraction [bp 160–165° (0.45 Torr)] yielded **2-*p*-*tert*-butylphenylthio-3,5-lutidine** (5.67 g, 24.4%): pmr ($CDCl_3$) δ 8.23 (m, H-6), 7.30 (m, H-4), 2.32 (3-CH_3), 2.20 (5-CH_3), 1.29 (*tert*-C_4H_9). *Anal.* Calcd for $C_{17}H_{21}NS$: N, 5.16. Found: N, 5.06.

The benzene solution was evaporated *in vacuo* and the residue recrystallized from 95% ethanol to give the disulfide (10.17 g, 61.5%).

Reaction of 2,6-Lutidine 1-Oxide and Thiophenol with Benzenesulfonyl Chloride (Method C).—Distillation of the basic fraction yielded 2,6-lutidine 1-oxide, 2.61 g [bp 75–76° (0.15 Torr)], and the sulfides, 7.74 g [bp 109–112° (0.15 Torr)]. Elution from Woelm alumina by petroleum ether furnished **3-phenylthio-2,6-lutidine** (R_f 0.35): pmr ($CDCl_3$) δ 7.58 (H-4), 7.01 (H-5), 2.63 (6-CH_3), 2.53 (2-CH_3) ($J_{4,5}$ = 8.2 Hz). *Anal.* Calcd for $C_{13}H_{13}NS$: N, 6.51. Found: N, 6.50. Subsequent elution by ether afforded **4-phenylthio-2,6-lutidine** (R_f 0.20): pmr ($CDCl_3$) δ 6.81 (H-3, H-5), 2.45 (2-, 6-CH_3). *Anal.* Calcd for $C_{13}H_{13}NS$: N, 6.51. Found: N, 6.45. Integration of the CH_3 peaks at δ 2.53, 2.63, and 2.45 on the 50-Hz sweep-width indicated the isomer distribution to be 82% of the 3 isomer and 18% of the 4 isomer, in 36% yield, based on the *N*-oxide.

From the benzene layer was isolated phenyl disulfide (6.20 g, 56.8%).

Reaction of 2,6-Lutidine 1-Oxide and *p*-*tert*-Butylthiophenol with Benzenesulfonyl Chloride (Method C).—Distillation of the basic fraction yielded the starting *N*-oxide, 5.98 g [bp 80–83° (0.80 Torr)], and the sulfides, 3.50 g (11.7%) [bp 152–154° (0.40 Torr)]. **3-*p*-*tert*-Butylphenylthio-2,6-lutidine** was eluted from alumina by petroleum ether–benzene (1:1): pmr ($CDCl_3$) δ 7.56 (H-4), 7.42 (m, 4-Ar H), 7.04 (H-5), 2.66 (6-CH_3), 2.55 (2-CH_3), 1.30 (*tert*-C_4H_9) ($J_{4,5}$ = 8.2 Hz). *Anal.* Calcd for $C_{17}H_{21}NS$: N, 5.16. Found: N, 5.09.

Further elution with the same solvent afforded pure **4-*p*-*tert*-butylphenylthio-2,6-lutidine**: pmr ($CDCl_3$) δ 7.62 (m, 4-Ar H), 6.83 (H-3, H-5), 2.45 (2-, 6-CH_3), 1.36 (*tert*-C_4H_9). *Anal.* Calcd for $C_{17}H_{21}NS$: N, 5.16. Found: N, 5.11. Based on the *N*-oxide the yield of sulfides was 11.7% with the ratio of 3 to 4 isomers being 83:17. The disulfide was also isolated in 82% yield.

Reaction of 2,4,6-Collidine 1-Oxide and Thiophenol with Benzenesulfonyl Chloride (Method C).—Distillation of the basic fraction yielded the starting oxide, 6.55 g, 47% recovery [bp 96–99° (0.15 Torr)], and **3-phenylthio-2,4,6-collidine** [5.0 g, 9.5%, bp 127–129° (0.15 Torr)], which was purified conveniently by passing through alumina in petroleum ether: pmr ($CDCl_3$) δ 7.00–7.87 (m, 5-Ar H, H-5), 2.71 (2-CH_3), 2.57 (6-CH_3), 2.41 (4-CH_3). *Anal.* Calcd for $C_{14}H_{15}NS$: N, 6.11. Found: N, 6.21.

Reaction of Lepidine 1-Oxide and Thiophenol with Methanesulfonyl Chloride (Method B).—Distillation of the basic fraction yielded lepidine [1.88 g, bp 80–82° (0.25 Torr)] and the sulfides [12.87 g, 51.3%, bp 162–164° (0.20 Torr)]. Elution from alumina by petroleum ether–benzene (1:1) furnished **2-phenylthiolepidine**: pmr ($CDCl_3$) δ 7.25–8.08 (m, 9-Ar H), 6.85 (CH_3) (J_{3,CH_3} = 0.9 Hz). *Anal.* Calcd for $C_{16}H_{13}NS$: N, 5.57. Found: N, 5.50. Elution with benzene–ether (1:1) afforded **3-phenylthiolepidine**: pmr ($CDCl_3$) δ 8.88 (H-2), 7.60–8.31 (4-quinolyl H), 7.21 (s, 5-Ar H), 2.79 (CH_3). *Anal.* Calcd for $C_{16}H_{13}NS$: N, 5.57. Found: N, 5.47. The distribution (pmr) was 83:17 for 2 and 3 isomers.

The remaining benzene layer was evaporated *in vacuo* and the residue recrystallized from 95% ethanol to give phenyl disulfide (3.84 g, 35.2%).

Based on these results the yield of the arylthiolepidines was 51.3%.

Reaction of Pyridine 1-Oxide and Ethyl Thioglycolate with Benzenesulfonyl Chloride (Method C).—To a stirred ice-cold solution of methanesulfonyl chloride (50 ml) and pyridine 1-oxide (9.5 g, 0.1 mol) was added ethyl thioglycolate (24 g, 1.0 mol). The temperature rose sharply to 90° and remained there for 5 min and then fell slowly to 40°. A low-boiling fraction was removed [68.6 g, bp 28–31° (0.2 Torr)] and was not examined further. Its pmr spectra showed no aromatic signals. The semisolid residue was worked up for the basic fraction. Purification of the fraction by means of gc (SE-30 column, injection temperature 70°) afforded **ethyl (2-pyridinethio)acetate** (14.2% based on *N*-oxide, rt 82.0 min): bp 92–96° (0.1 Torr); pmr ($CDCl_3$) δ 1.23 (t, CH_3), 3.90 (s, CH_2), 4.13 (q, CH_2), 8.38 (H-6) ($J_{3,6}$ = 1.0, $J_{4,6}$ = 1.8, $J_{5,6}$ = 4.8 Hz); mass spectral parent peak (70 eV) at *m/e* 197. *Anal.* Calcd for $C_9H_{11}NO_2S$: N, 7.10. Found: N, 7.07.

Reaction of 4-Picoline 1-Oxide and Ethyl Thioglycolate with Benzenesulfonyl Chloride (Method C).—Work-up in the usual manner provided **ethyl (4-methyl-2-pyridinethio)acetate** [0.95 g, bp 109–111° (0.1 Torr)] which was purified on a column of alumina (eluted by petroleum ether–benzene, 1:1): pmr ($CDCl_3$) δ 8.27 (H-6), 7.08 (H-3), 6.81 (H-5), 4.11 (q, CH_2), 3.93 (s, CH_2), 2.21 (s, CH_3), 1.18 (t, CH_3) ($J_{5,6}$ = 5.1 Hz). *Anal.* Calcd for $C_{10}H_{13}NO_2S$: N, 6.63. Found: N, 6.56.

Registry No.—2 (R = H; X = H), 3111-54-4; 2 (R = H; X = Cl), 28856-69-1; 2 (R = H; X = *tert*-C_4H_9), 28856-70-4; 2 (R = CH_3; X = H), 2732-48-1; 2 (R = CH_3; X = Cl), 28856-72-6; 2 (R = CH_3; X = *tert*-C_4H_9), 28856-73-7; 2 (R = *tert*-C_4H_9; X = H), 28856-74-8; 2 (R = *tert*-C_4H_9; X = Cl), 28856-75-9; 2 (R = *tert*-C_4H_9; X = *tert*-C_4H_9), 28856-76-0; 3 (R = H; X = H), 28856-77-1; 3 (R = H; X = Cl), 28856-78-2; 3 (R = H; X = *tert*-C_4H_9), 28856-79-3; 3 (R = CH_3; X = H), 28856-80-6; 3 (R = CH_3; X = Cl), 28856-81-7; 3 (R = CH_3; X = *tert*-C_4H_9), 28856-82-8; 3 (R = *tert*-C_4H_9; X = H), 28856-83-9; 3 (R = *tert*-C_4H_9; X = Cl), 28856-84-0; 3 (R = *tert*-C_4H_9; X = *tert*-C_4H_9), 28856-85-1; 2-*p*-*tert*-butylphenylthio-3,5-lutidine, 28957-70-2; 3-phenylthio-2,6-lutidine, 28856-86-2; 4-phenylthio-2,6-lutidine, 28856-87-3; 3-*p*-*tert*-butylphenylthio-2,6-lutidine, 28856-88-4; 4-*p*-*tert*-butylphenylthio-2,6-lutidine, 28856-89-5; 3-phenylthio-2,4,6-collidine, 28957-71-3; 2-phenylthiolepidine, 5460-87-2; 3-phenylthiolepidine, 28856-91-9; ethyl (2-pyridinethio)acetate, 28856-92-0; ethyl (4-methyl-2-pyridinethio)acetate, 28856-93-1.