Irradiations. A. Solid State.—Solid-state photodimerizations of the styrylpyridine methiodides and methosulfates were conducted as benzene suspensions according to the previous description.[3]

Solid-state photodimerizations of the styrylpyridine hydrochlorides were conducted in a manner similar to that described earlier,[3] except that the suspension medium used was heptane since certain of the 5-ethyl-2-styrylpyridinium salts show slight solubility in benzene and irradiations of the salts in solution generally promoted photoisomerization.

B. Solution. In previous work a Hanovia medium-pressure lamp was used. A more convenient method is as follows: In a typical irradiation, a solution of 10 g. (0.55 mole) of *trans*-2-styrylpyridine in a mixture of 10 ml. of concentrated hydrochloric acid and 1 l. of water was placed in a 2-l. evaporating dish. The solution was stirred by means of a Teflon-covered stirrer bar magnetically driven through the bottom of the dish. A GRS sunlamp was placed 12 in. above the surface of the solution. Periodically, aliquots were withdrawn and diluted with water to give 2.5×10^{-5} *M* solutions for ultraviolet examination. Prior to irradiation, the solution had the following characteristics: λ_{max} 328 mμ, ϵ 25,300. After 21 hr. of irradiation, the characteristics of the solution were: λ_{max} 264 mμ, ϵ 8,800, and λ_{max} 321 mμ, ϵ 4,640. The irradiation product was isolated in the manner described.[3]

Nitration of the Dimer of 2-Styrylpyridine (Ib): IVb.—A solution of 7.2 g. of the dimer of Ia (Ib) in 50 ml. of concentrated sulfuric acid was cooled to 10° in an ice bath and to this stirred solution was slowly added 2.6 ml. of concentrated nitric acid. The mixture was allowed to warm up to room temperature, poured into 250 ml. of ice–water, and made basic with ammonium hydroxide. The precipitated solid was collected, washed with water, and recrystallized from ethanol to yield 6.5 g. of product (IVb), m.p. 161–162°.

Anal. Calcd. for $C_{26}H_{20}N_4O_4$: C, 69.0; H, 4.4; N, 12.4. Found: C, 68.7; H, 4.5; N, 12.1.

Nitration of the Dimer of 5-Ethyl-2-styrylpyridine (Vb): IXb.—By the procedure described for IVb there was obtained from 8.4 g. of the dimer (Vb), 6 g. of the dinitro derivative (IXb), melting at 180°.

Anal. Calcd. for $C_{30}H_{28}N_4O_4$: C, 70.9; H, 5.5; N, 11.0. Found: C, 70.5; H, 5.7; N, 10.9.

Quaternization of IVb: Di(1-methyl-2-pyridinium)di(4-nitrophenyl)cyclobutane Iodide (IVd).—A mixture of 1 g. of IVb, obtained by nitration of the dimer of Ia (Ib), and 5 ml. of dimethyl sulfate was heated on a steam bath for 30 min. The solid that separated from the solution was collected, washed with ether, dissolved in 15 ml. of warm water, and 1 g. of potassium iodide was added to the solution. The solid that separated was collected and dried to yield 1.1 g. of the quaternary salt (IVd), m.p. 265°.

Anal. Calcd. for $C_{28}H_{26}N_4O_4I_2$: C, 45.7; H, 3.5; N, 7.6. Found: C, 46.0; H, 3.5; N, 8.0.

Quaternization of IXb: Di(1-methyl-5-ethyl-2-pyridinium)-di(4-nitrophenyl)cyclobutane (IXd).—The preparation of IXd was carried out by the procedure used for the quaternization of IVb. The dimer IXd melted at 245–246°.

Anal. Calcd. for $C_{32}H_{34}N_4O_4I_2$: C, 48.5; H, 4.3; N, 7.1. Found: C, 48.3; H, 4.0; N, 7.3.

The Chemistry of Pyridine. I. Nucleophilic Substitution of 1-Alkoxypyridinium Salts by Mercaptide Ions

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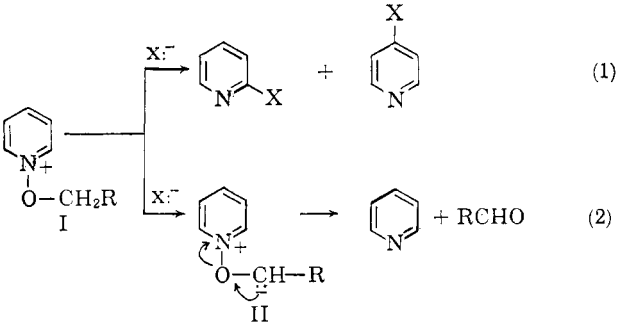
The reaction of 1-alkoxypyridinium salts with propyl- and octylmercaptide ions is described. In each instance, the product consisted of pyridine and a mixture of 3- and 4-alkylmercaptopyridines, predominantly the 3-isomer. These reactions are discussed in the light of existing knowledge of nucleophilic attack on pyridine N-oxides. Unequivocal syntheses of the corresponding 2-, 3-, and 4-alkylmercaptopyridines as reference compounds is reported.

Current interest is centered on the use of pyridine N-oxide and 1-alkoxypyridinium salts as intermediates for the synthesis of substituted pyridines.[2] Nucleophilic substitution in the 1-alkoxypyridinium cation, I, has received considerable attention recently. It was shown that cyanide ion (X = CN) reacted with these salts to form 2- and 4-pyridinecarbonitriles[3] (equation 1) and no substitution was observed at the 3-position of the pyridine ring. The reaction of Grignard reagents with 1-alkoxypyridinium salts was reported recently to yield only 2-substituted pyridines and apparently substitution did not occur at the 3- or 4-position of the ring.[4] These authors offer a mechanism which satisfactorily accounts for the formation of the 2- and 4-substituted pyridines (equation 1).



In our studies, we treated 1-alkoxypyridinium salts with mercaptide and thiophenoxide ions with the aim of introducing the alkyl- and arylmercapto group into the pyridine ring. Initially, this reaction was explored with the anions of propyl- and octylmercaptide ions and these were found to effect substitution in the pyridine ring to yield the corresponding alkylmercaptopyridines. The reaction of 1-ethoxypyridinium ethyl sulfate with sodium *n*-propylmercaptide was studied in some detail and is presented first. When this reaction was conducted in a mixture of 1-propanethiol and ethanol (10:1) two major fractions were obtained. The first one was identified as pyridine (70%). This product can arise from nucleophilic attack at the α-carbon of the 1-alkoxy side chain *via* the intermediate, II, which decomposes to pyridine and an aldehyde (equation 2).[5]

(1) Taken from the Ph.D. thesis of Libero A. Gardella, University of Illinois at the Medical Center, Chicago 12, Ill., June, 1962.

(2) For recent reviews on this topic, see (a) D. V. Ioffe and L. S. Eiros, *Russ. Chem. Rev.* (*Eng. Transl.*), **30**, 569 (1961); (b) K. Thomas and D. Jerchel, in W. Foerst's "Neuere Methoden der Präparativen Organischen Chemie," Band III, Verlag Chemie, GmbH, Weinheim/Bergstr., 1961, p. 61; (c) A. R. Katritzky and J. M. Lagowski, "Heterocyclic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1960, pp. 61, 102; (d) E. N. Shaw, "Pyridine and Its Derivatives, Part Two," E. Klingsberg, ed., Interscience Publishers, Inc., New York, N. Y., 1961, Chap. IV, pp. 97–153.

(3) (a) W. E. Feeley and E. M. Beavers, *J. Am. Chem. Soc.*, **31**, 4004 (1959); (b) H. Tani, *Chem. Pharm. Bull., Japan*, **7**, 930 (1959); *J. Pharm. Soc., Japan*, **81**, 141 (1961), and papers quoted therein.

(4) O. Cervinka, *Collection Czech. Chem. Commun.*, **27**, 567 (1962).

The higher boiling fraction was a colorless oil with correct analysis for a propylmercaptopyridine (30% yield) but proved to be a mixture of isomers which could not be separated by distillation. However, by means of chromatography on alumina, this mixture was resolved into 3- and 4-propylmercaptopyridines, with the 3-isomer being the dominant constituent (6:1). The 2-isomer could not be detected in the mixture although it was one of the expected products (equation 1). Whereas the formation of the 4-pyridyl sulfide can be explained by the mechanism proposed for the nucleophilic attack of cyanide on I, it is difficult at present to rationalize the formation of the 3-isomer. Although β-substitution has been observed when pyridine N-oxides were treated with a variety of reagents, the reactions are not comparable.[6] Further experiments are planned to gain insight into the mechanism of the reaction of I with mercaptide ion.

A number of attempts were made to improve the total yield or change the nature of the products in the reaction of I with mercaptide ion. Since the reactants are ionic species, the nature of the solvent was thought to play an important role. This aspect was investigated with varying results. When 1-ethoxypyridinium ethyl sulfate was added to sodium *n*-propylmercaptide in 1-propanethiol, a heterogeneous mixture resulted. The mixture of propylmercaptopyridines did not change materially whether the reaction was heated at the reflux for 0.5 or 24 hours (22 and 27% yield, respectively). Although the yield did not change materially, the product proved to be a cleaner one when to this reaction mixture some ethanol (1/10 of the volume of thiol) was added. However, as the amount of ethanol to thiol was increased (1:1) the yield of sulfides dropped to 9% while the reaction in ethanol furnished barely 1% yield.

We also turned our attention to explore other solvent media for this reaction. The reaction between 1-ethoxypyridinium ethyl sulfate and two moles of sodium *n*-propylmercaptide in either tetrahydrofuran (1 hour of reflux) or toluene (23 hours of reflux), yielded in each case only 8% of the mixture of sulfides and pyridine was isolated in 70 and 60%, respectively. The yield of the sulfide mixture was only 5% when the reaction was conducted in a non-acidic yet polar medium such as N,N-dimethylformamide (100°, 0.5 hours) while in a basic medium such as triethylamine (100°, 5 hours) the sulfides were formed in 18% yield. Since two possible competing reactions can occur between the 1-ethoxypyridinium cation and the mercaptide ion (equations 1 and 2, attack on the ring or alkoxy side chain, respectively) it was sought to minimize or eliminate the latter by increasing the size of the N-alkoxy side chain.[3b] Thus, the reaction of 1-butoxypyridinium benzenesulfonate with sodium *n*-propylmercaptide in propanethiol containing some ethanol (4:1) at 100° for two hours yielded 23% of the sulfides and only 1.5% of pyridine. Although the formation of pyridine by nucleophilic attack on the side chain was inhibited in the last reaction, the substitution by mercaptide ion was not greatly enhanced.

The reaction of 1-ethoxypyridinium ethyl sulfate with sodium *n*-octylmercaptide in a mixture of 1-octanethiol and ethanol (10:1 by volume) was also studied. This reaction yielded a mixture of 3- and 4-octylmercaptopyridines (6.7%) and pyridine (12.7%) as identified by means of infrared spectroscopy. Interestingly enough, the reaction of 1-ethoxypyridinium ethyl sulfate with sodium thiophenoxide in thiophenol did not furnish a detectable amount of phenylmercaptopyridines. The only product of the reaction which could be identified was pyridine (25%). No explanation is offered at present why the thiophenoxide ion failed to effect nuclear substitution.

Experimental[7]

Synthesis of Reference Compounds.—2- and 4-Alkylmercaptopyridines were prepared by the direct displacement of the corresponding halo group by alkylmercaptide ion. The solvent of choice was N,N-dimethylformamide and the procedure of Profft[8] was modified by substituting sodium hydride for potassium hydroxide as the base.

2-Propylmercaptopyridine.—1-Propanethiol[9] (7.6 g.; 0.1 mole) was added dropwise with stirring, to a suspension of sodium hydride (2.4 g.; 0.1 mole) in N,N-dimethylformamide (40 ml.). After the evolution of hydrogen had ceased, 2-chloropyridine[10] (11.35 g., 0.1 mole) was added and the mixture refluxed in an oil bath for 4.0 hr. The reaction mixture was cooled, acidified with 10% hydrochloric acid, and the solvents were removed by distillation *in vacuo*. Water (200 ml.) was added to the residue and the solution extracted with a 1:1 ether–benzene solution (four 50-ml. portions). The aqueous layer was made basic with a 20% sodium hydroxide solution and extracted with methylene chloride (eight 50-ml. portions). Distillation of the methylene chloride extract furnished 2-propylmercaptopyridine (3.1 g.; 20%), b.p. 108–110° (18 mm.). This sulfide had previously been made from the reaction of 2-mercaptopyridine and 1-bromopropane in 62% yield and its b.p. was recorded at 53–55° at 1 mm.[11]

The **picrate** was crystallized from ethanol, m.p. 122–123° (lit.,[11] m.p. 124–125°).

4-Propylmercaptopyridine.—This **sulfide** was prepared in the same manner as above from 4-chloropyridine (11.35 g.; 0.1 mole) and 1-propanethiol (7.6 g.; 0.1 mole) with the modification that the mixture was heated on a steam bath for 4.0 hr. The sulfide boiled between 130–133° at (16 mm.) and weighed 12.2 g. (80%), $n^{25}D$ 1.5632.

Anal. Calcd. for $C_8H_{11}NS$: C, 62.70; H, 7.24; N, 9.14. Found: C, 62.65; H, 7.05; N, 9.23.

(5) This reaction is quite a general one and for examples of it see, (a) W. E. Feeley, W. L. Lehn, and V. Boekelheide, *J. Org. Chem.*, **22**, 1135 (1957), and references quoted therein; (b) A. R. Katritzsky, *J. Chem. Soc.*, 2408 (1956); (c) J. M. Tien, I. M. Hunsberger, and A. M. Javallans, Abstracts of the 135th National Meeting of the American Chemical Society, Boston, Mass., April, 1959, p. 76-O; (d) C. H. Depuy and E. F. Zaweski, *J. Am. Chem. Soc.*, **81**, 4920 (1959). This reaction proceeds readily at 0° and has been utilized in the synthesis of aromatic aldehydes,[5a] glyoxylic esters,[5c] and cyclopentene-3,5-dione.[5d] In these instances, the nucleophile, X, was the hydroxide ion.

(6) To explain β-substitution, a mechanism has been proposed by (a) E. Ochiai and M. Ikehara, *Pharm. Bull., Japan*, **3**, 454 (1955); (b) M. M. Robison and B. L. Robison, *J. Org. Chem.*, **21**, 1337 (1957). For example, the reaction of isoquinoline 2-oxide with acetic anhydride gives (after hydrolysis) mainly 1-isoquinolinol (53%) and a smaller quantity of 4-isoquinolinol (8.9%),[6b] while 3-chloroisoquinoline 2-oxide with the same reagent produces mainly 3-chloro-4-isoquinolinol (61%) with less than 1% of the expected 3-chloro-1-isoquinolinol [M. M. Robison and B. L. Robison, *J. Am. Chem. Soc.*, **80**, 3443 (1958)]. Furthermore, the reaction of *p*-toluenesulfonyl chloride with pyridine N-oxide yields (among other products) mainly 3-*p*-toluenesulfonyloxypyridines [M. Marakami and E. Matsumura, *Chem. Abstr.*, **45**, 4698 (1951); **47**, 1745 (1953); E. Matsumura, *ibid.*, **48**, 6442 (1954); H. J. den Hertog, D. J. Buurman, and P. A. deVilliers, *Rec. trav. chim.*, **80**, 325 (1961)]. Exclusive β-substitution was observed when isoquinoline 2-oxide was treated with *p*-toluenesulfonyl chloride to give 4-*p*-toluenesulfonyloxyisoquinoline only.[6a]

(7) All melting points and boiling points are uncorrected. Microanalyses were performed by Micro-Tech Laboratories, Skokie, Ill., and Dr. Kurt Eder, Geneva, Switzerland. Some of the nitrogen analyses were performed using a Coleman Nitrogen Analyzer, Model 29.

(8) E. Profft and W. Rolle, *J. prakt. Chem.*, (4) **11**, 22 (1960).

(9) We gratefully acknowledge the generous gift of this chemical from (a) Pennsalt Chemicals Corp., Philadelphia, Pa.; (b) Phillips Petroleum Co., Bartlesville, Okla.

(10) Purchased from Aldrich Chemical Company, Milwaukee, Wis.

(11) D. S. Tarbell and M. A. McCall, *J. Am. Chem. Soc.*, **74**, 48 (1952).

p-**Toluenesulfonate** crystallized from acetone, m.p. 110–112°.

Anal. Calcd. for $C_{15}H_{19}NO_3S_2$: C, 55.36; H, 5.88; N, 4.30; Found: C, 55.33; H, 5.82; N, 4.27.

The **picrate** was recrystallized from ethanol, m.p. 134–136°. This salt was found to be sensitive to light and turned dark in it.

Anal. Calcd. for $C_{14}H_{14}N_4O_7S$: N, 14.65. Found: N, 14.62.

2-Octylmercaptopyridine.—This **sulfide** was prepared in the same manner as described for 2-propylmercaptopyridine from 2-chloropyridine (5.78 g.; 0.05 mole) and 1-octanethiol[9a] (7.30 g.; 0.05 mole). The product distilled at 113–115° (2.0 mm.) and weighed 3.0 g. (27%).

Anal. Calcd. for $C_{13}H_{21}NS$: C, 69.90; H, 9.48; N, 6.27. Found: C, 70.05; H, 9.25; N, 6.14.

The **picrate** was crystallized from ethanol, m.p. 77–78°.

Anal. Calcd. for $C_{19}H_{24}N_4O_7S$: N, 12.38. Found: N, 12.25.

4-Octylmercaptopyridine.—This **sulfide** was synthesized as described for the 4-propyl analog from 4-chloropyridine (2.84 g.; 0.025 mole) and 1-octanethiol (3.65 g.; 0.025 mole). The fraction which was collected weighed 3.2 g. (57.5%) and boiled at 127–129° (2.0 mm.).

Anal. Calcd. for $C_{13}H_{21}NS$: C, 69.90; H, 9.48; N, 6.27. Found: C, 69.91; H, 9.33; N, 6.43.

The **picrate** (from ethanol) melted between 110–113°.

Anal. Calcd. for $C_{19}H_{24}N_4O_7S$: N, 12.38. Found: N, 12.50.

3-Propylmercaptopyridine from 3-Aminopyridine.—The synthesis of this sulfide was adapted from that outlined by Albert[12] for his synthesis of 3-benzoylthioquinoline from 3-aminoquinoline.

Sodium nitrite (8.5 g.; 0.1 mole) in water (20 ml.) was added dropwise, with stirring, to a solution of 3-aminopyridine (9.4 g.; 0.1 mole) in concentrated hydrochloric acid (21 ml.) and ice (21 g.), the temperature being kept between −5 and 0°. The solution of the diazonium salt was added slowly to a solution of potassium ethyl xanthate[13] (22 g.; 0.14 mole) in water (25 ml.) at 40–50°. When the addition was completed, the mixture was heated to 80°, cooled and extracted with ether (five 100-ml. portions). Ether was removed *in vacuo* and no attempt was made to isolate ethyl 3-pyridyl xanthate, but rather the residue was hydrolyzed immediately by boiling it with potassium hydroxide (15 g.; 0.25 mole) in 95% ethanol (125 ml.) for 23 hr. The intermediate thiol was not isolated but alkylated in the basic medium by the addition of 1-iodopropane (51 g.; 0.3 mole). Heating at reflux was continued for an additional 4.0 hr. and the reaction mixture then acidified with concentrated hydrochloric acid. Solvents were removed *in vacuo*, the residue was dissolved in water (500 ml.) and extracted with a 1:1 ether–benzene solution (four 100-ml. portions). The aqueous layer was made basic with a 20% sodium hydroxide solution, extracted with methylene chloride (five 200-ml. portions) and this extract was distilled. The **sulfide** (4.25 g.; 28% based on 3-aminopyridine), boiled at 124–128° (16 mm.), $n^{26}D$ 1.5548.

Anal. Calcd. for $C_8H_{11}NS$: C, 62.70; H, 7.24; N, 9.14. Found: C, 62.80; H, 7.13; N, 8.99.

The **picrate** melted between 113–115° (from ethanol).

Anal. Calcd. for $C_{14}H_{14}N_4O_7S$: N, 14.65. Found: N, 14.40.

An attempt to prepare this sulfide from 3-chloropyridine proved abortive. By heating this halo compound with sodium *n*-propylmercaptide neat at 175° for 36 hr. led to the recovery of 60% of 3-chloropyridine as the only recognizable product.

3-Octylmercaptopyridine from 3-Pyridinesulfonic Acid.—The sulfonic acid was converted to the sulfonyl chloride[14] which was reduced to the 3-pyridinethiol hexachlorostannate.[15] This double salt (4.44 g.; 0.01 mole) was dissolved in 10% sodium hydroxide solution (40 ml.). 1-Iodoöctane (4.8 g., 0.02 mole) was added to this solution and the mixture first stirred at room temperature for 1.5 hr., then at 100° for 2.5 hr. The reaction mixture was extracted with methylene chloride (150 ml.) and this extract shaken with 1:3 hydrochloric acid (200 ml.), but treatment with base of the acidic aqueous phase did not yield a product. Since the methylene chloride layer might have dissolved the product (possibly as its hydrochloride) the methylene chloride solution was shaken with 10% sodium carbonate, and then distilled. The **sulfide** was obtained, b.p. 122–124° at 0.4 mm. It weighed 2.3 g. (50%). It was redistilled for analysis, b.p. 120° at 0.1 mm.

Anal. Calcd. for $C_{13}H_{21}NS$: C, 69.90; H, 9.48; N, 6.27. Found: C, 70.08; H, 9.30; N, 6.31.

Its **picrate** crystallized from ethanol, m.p. 91°.

Anal. Calcd. for $C_{19}H_{24}N_4O_7S$: N, 12.38. Found: N, 12.06.

1-Ethoxypyridinium Ethyl Sulfate.—The method for the preparation of 1-methoxypyridinium methyl sulfate as described by Feeley and Beavers[3a] was adapted. Unlike the 1-methoxy analog, this salt was exceedingly difficult to crystallize. Usually, a gum was obtained and was used as such immediately in the next step. Although it was induced to crystallize once on prolonged scratching, it was even to hygroscopic to insert into a melting point tube. The salt was characterized by its picrate which crystallized from ethanol by the addition of a 1:1 solution of ether and hexane, m.p. 76–78° (lit.,[4] m.p. 76–76.5°).

Reaction of 1-Ethoxypyridinium Ethyl Sulfate with Sodium *n*-Propylmercaptide.—Sodium hydride [4.8 g.; 0.2 mole (9.2 g. of a 53.2% suspension in mineral oil as obtained from Metal Hydrides, Inc., Beverly, Mass.)], was added slowly, with stirring, to 1-propanethiol (76 g.; 1.0 mole) contained in a 1-l. flask. (Since it was observed that the mixture foamed considerably during the reaction, it is advisable to use a large vessel.) To this stirred suspension of sodium *n*-propylmercaptide in 1-propanethiol was added 1-ethoxypyridinium ethyl sulfate as a sirup (pre-

TABLE I

INFRARED ABSORPTION BANDS (CM.$^{-1}$) OF 2-, 3-, AND 4-ALKYLMERCAPTOPYRIDINES

In chloroform

—Propylmercaptopyridines—			—Octylmercaptopyridines—		
2-[a]	3-	4-	2-	3-	4-
	3305 w-b[b]	3275 w-b[b]		3300 vw-b[b]	3275 vw-b[b]
3038 m	3081 sh	3076 sh			
2970 vs	2974	2964			2959 sh
2930 s			2935 vs	2920 vs	2935 vs
2861 s	2876 s	2866 s	2861 s	2851 s	2861 vs
	2492 vw-b	2467 w		2492 vw-b	2467 w-b
					2261 vw
		1931 w			1931 vw-b
					1676 vw-b
1582 vs	1580 s	1580 vs	1580 vs	1578 m	1583 vs
1560 s	1565 s		1560 s	1565 m	
		1542 s			1543 s
	1470 vs	1486 vs			1485 s
1452 vs		1465 s	1456 vs	1471 vs	1468 s
	1440 vw	1440 m			1441 w
		1427 m			1431 w
1414 vs	1408 vs	1412 vs	1417 vs	1408 s	1413 s
1378 m	1382 m	1381 m	1381 w	1379 w	1381 w
	1340 vw	1341 vw			
	1322 vw	1321 vw			1321 vw
1291 s	1293 m	1288 m			1294 vw-b
1279 s			1282 m		1265 vw-b
1238 s	1238 s-b	1242 s	1241 w	1242 m-b	1240 m
	1187 w			1184 w	
			1145 s		
1126 vs-b	1121 s		1124 vs	1122 m	
	1111 s	1111 s-b		1109 s	1111 s-b
1096 m	1096 s	1096 sh		1091 m	
	1052 vw	1065 s			1066 m
1041 s	1035 m	1049 vw	1043 m	1034 w	
	1019 s			1019 s	
		994 sh			998 sh
982 s		984 s	984 m		985 s
897 w	897 w	897 w			
	803 s	807 s			809 s

Absorption bands between 700 and 800 cm.$^{-1}$ in carbon disulfide

	798 s	799 vs		790 s	797 vs
756 vs			759 vs		
		743 sh			740 sh
732 m	731 sh				
726 s		728 m	729 s	727 sh	726 m
	710 s	714 s		710 vs	710 s

[a] The sulfide has been recorded previously as a liquid film.[11] [b] This broad band was absent in the spectrum determined in chloroform from which ethanol had been removed nor was it present in the spectrum in carbon tetrachloride or carbon disulfide. This band was observed in the spectra of 3- and 4-substituted, but absent in 2-substituted pyridines even when recorded in spectral grade chloroform. Since chloroform is stabilized by ethanol, this broad band is attributed to the OH stretching frequency, the hydroxyl group bonded to the ring nitrogen atom of the less hindered 3- and 4-substituted pyridines.

(12) A. Albert and G. B. Barlin, *J. Chem. Soc.*, 2384 (1959).

(13) C. C. Price and G. W. Stacy, *Org. Syn.*, **28**, 82 (1948); the displacement of the diazonium group by the ethyl xanthate ion has recently been reinvestigated in detail by J. R. Cox, *et al.*, *J. Org. Chem.*, **25**, 1083 (1960).

(14) H. G. Machek, *Monatsh.*, **72**, 84 (1939).

(15) N. Steiger, British Patent 637,130 (May 10, 1959); *Chem. Abstr.*, **44**, 8380 (1950).

pared as above). The heterogeneous mixture did not show signs of reaction. After stirring this mixture for 5.0 min., ethanol (10 ml.) was added and the reaction mixture began to reflux vigorously and foamed considerably. When the foaming lessened, the reaction mixture was refluxed an additional 0.5 hr. on a steam bath, cooled and acidified with 10% hydrochloric acid and most of the solvent removed by distillation *in vacuo*. The residue was treated with water (300 ml.) and extracted with a 1:1 benzene–ether solution (four 100-ml. portions). The aqueous layer was then made basic with a 20% solution of sodium hydroxide, extracted with methylene chloride (five 200-ml. portions). After methylene chloride had been distilled, the residue was fractionated (the receiver placed in a 1:1 chloroform–carbon tetrachloride and Dry-ice bath) to yield pyridine (5.5 g.; 69.6% based on pyridine 1-oxide), b.p. 30–40° (16 mm.) and a mixture of 3- and 4-propylmercaptopyridines, (4.91 g.; 32.1% based on pyridine 1-oxide), b.p. 64–68° (1 mm.). Infrared spectra confirmed the presence of 3- and 4-isomers.

Anal. Calcd. for $C_8H_{11}NS$: C, 62.70; H, 7.24; N, 9.14. Found: C, 62.56; H, 7.34; N, 8.86.

The fraction containing the mixture of 3- and 4-propylmercaptopyridines (4.91 g.) was placed on a column of alumina (100 g.; Alcoa activated alumina, grade F-20) in petroleum ether (10 ml.), b.p. 30–60°. The column was eluted with petroleum ether (b.p. 30–60°) with 500-ml. portions. The residue of each fraction was examined by its infrared spectrum, and carefully scrutinized for its components using the infrared spectra of pure 2-, 3- and 4-propylmercaptopyridines (recorded in Table I) as references. In particular, each fraction was examined for the presence of small quantities of isomeric impurities. For this purpose certain strong bands in the spectrum of each isomer were chosen. The first eluates from the column contained only the 3-isomer, characterized by strong sharp band at 1019 cm.$^{-1}$ which is apparently featured in many 3-substituted pyridines.[16] If the 2- and/or 4-isomers were present in these fractions, the presence of them would have been detected by absorption near 980 cm.$^{-1}$ since both isomers possess strong bands there. Furthermore, the 2- and 4-isomers show very strong bands near 1580 compared to a much weaker band at 1577 cm.$^{-1}$ for the 3-isomer. To distinguish if the 2- or the 4-isomer was the only contaminant, use of the overall patterns of the 2- and 4-isomers was made. The most distinguishing feature between these two isomers was the very strong band at 1452 for the 2-isomer, the strong band at 1465 cm.$^{-1}$ for the 4-isomer. Further elution then afforded the pure 4-isomer, free from 2- and 3-isomers shown by the absence of the 1452- and 1019-cm.$^{-1}$ bands, respectively.

In this particular experiment, 4500 ml. of petroleum ether eluted only 3-propylmercaptopyridine (4.50 g.; prior to distillation) which boiled between 123–124° at 16 mm., and weighed 4.1 g. (26.8% based on pyridine 1-oxide). Its refractive index ($n^{26}D$ 1.5550) and infrared spectrum were identical to the authentic sample made from 3-aminopyridine. Furthermore, its picrate (m.p. 113–115°) did not depress that made from the authentic sample.

Further elution of the column with anhydrous benzene (in 100-ml. portions, checking each fraction for its contents by means of infrared spectroscopy; a total of 200 ml.) yielded 4-propylmercaptopyridine (0.7 g.) which when distilled, b.p. 128–130° at 16 mm., weighed 0.55 g. (3.6% based on pyridine 1-oxide). Its infrared spectrum was identical to that of the sample made from 4-chloropyridine.

Reaction of 1-Ethoxypyridinium Ethyl Sulfate and Sodium *n*-Octylmercaptide.—Sodium hydride [4.8 g.; 0.2 mole (9.2 g. of a 53.2% suspension in mineral oil)] was added slowly in very small portions, with stirring, to 1-octanethiol (146 g.; 1.0 mole) contained in a 1-l. flask. Extreme care must be taken during the addition of sodium hydride to the 1-octanethiol, since the reaction is extremely exothermic and there is a tendency to char the sodium *n*-octylmercaptide. To the stirred suspension of sodium *n*-octylmercaptide in 1-octanethiol was added the gummy 1-ethoxypyridinium ethyl sulfate prepared from pyridine 1-oxide (9.5 g., 0.1 mole) as previously described. The rest of the procedure was the same as described. On work-up of the reaction mixture the fractions collected were pyridine, b.p. 30–40° (20 mm.), 1.0 g. (12.7%), and the 3- and 4-octylmercaptopyridines, b.p. 114–118° (2 mm.), 1.5 g. (6.7%). The presence of the mixture of the two isomeric sulfides was proven by the analysis of the infrared spectrum as evident from the strong bands at 1019 and 809 cm.$^{-1}$.

Anal. Calcd. for $C_{13}H_{21}NS$: C, 69.90; H, 9.48; N, 6.27. Found: C, 69.71; H, 9.32; N, 6.29.

This mixture afforded a picrate which crystallized from ethanol to a constant m.p. 83–85° which is below the melting points of the picrates of either the 3- and 4-isomers.

Anal. Calcd. for $C_{19}H_{24}N_4O_7S$: N, 12.38. Found: N, 12.09.

When 1.0 g. of this mixture was placed on 20 g. of alumina (Alcoa, grade F-20), no sulfide was eluted with petroleum ether (b.p. 30–60°). However, each fraction (25-ml. portions; 675 ml. in all) eluted with 10% benzene in petroleum ether or benzene alone consisted only of mixture of the 3- and 4-isomers. The absence of the 2-isomers was established since all fractions did not show bands at 1456, 1043 and 984 cm.$^{-1}$ (see Table I).

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(16) It had been shown that 3-substituted pyridines absorb in the vicinity of 1020 cm.$^{-1}$ [A. R. Katritzky, A. R. Hands, and R. A. Jones, *J. Chem. Soc.*, 3165 (1958)]. For example, 3-chloropyridine absorbs at 1025, 3-aminopyridine at 1010, 3-nitropyridine at 1021, and 3-acetylpyridine at 1023 cm.$^{-1}$.

The Chemistry of Pyridine. II. The Reaction of 1-Alkoxypicolinium Salts with Mercaptide and Thiophenoxide Ions

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The reaction of 1-alkoxy-2- and 4-picolinium salts with thiophenoxide ion furnished 2- and 4-[(arylmercapto)-methyl]pyridines, respectively, but no nuclear substitution was observed. However, the similar reaction with mercaptide ion was considerably more complex. It was found that 1-alkoxy-4-picolinium salts with mercaptide ions yielded besides 4-[(alkylmercapto)methyl]pyridine also 2- and 3-alkylmercapto-4-picolines and 1,2-di(4-pyridyl)ethane. Explanations are rendered for the formation of these various products. Syntheses of a number of these thioethers as reference compounds are described.

Nucleophilic attack by mercaptide ion on 1-alkoxypyridinium salts gave rise to a mixture of pyridine and 3- and 4-alkylmercaptopyridines.[2] However, thiophenoxide ion, under identical conditions, yielded only pyridine and no arylmercaptopyridines could be detected.[2] Pyridine produced in these reactions arises

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(2) L. Bauer and L. A. Gardella, part I, *J. Org. Chem.*, **28**, 1320 (1963).