The Chemistry of Pyridine. V. Ring Substitution of Picoline and Methylpyrazine N-Oxides by Mercaptans[1,2]

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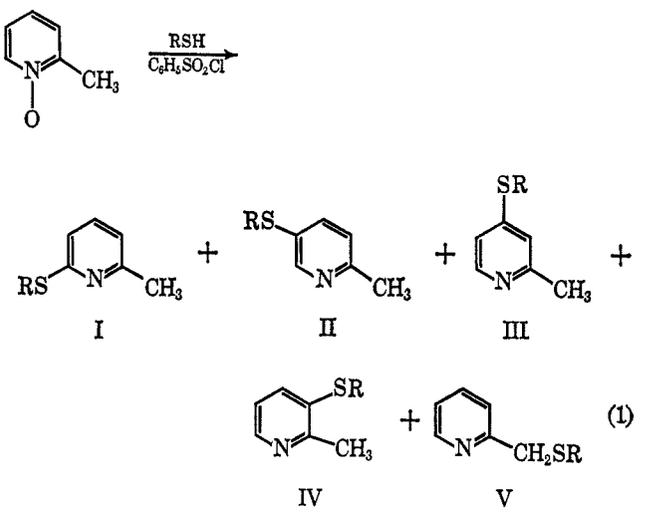
The reaction of each of the three isomeric picoline N-oxides with 1-propanethiol in the presence of benzenesulfonyl chloride produced a number of isomeric propylmercaptopicolines. Entry of the sulfide group took place at α- and β-ring positions and the methyl group seemed to exert little directive influence on this substitution. When 4-picoline 1-oxide was treated with 1-propanethiol in hot acetic anhydride, only the ring-substituted sulfides, *viz.*, 2- and 3-propylmercaptopicolines, were isolated. A similar reaction of 2,5-dimethylpyrazine mono- and di-N-oxides with 1-propanethiol in acetic anhydride gave 2,5-dimethyl-3-propylmercapto- and 2,5-dimethyl-3,6-dipropylmercaptopyrazines, respectively.

Previous work[3] has shown that the reaction of sodium *n*-propylmercaptide with 1-ethoxy-4-picolinium ethyl sulfate yielded a mixture of the 2-, 3- and ω-propylmercapto-4-picolines (X, XI, and XII). It was evident that during that reaction considerable substitution occurred in the active methylene group as well as in the ring. More recently, it was found that pyridine 1-oxide, *via* its 1-arenesulfonyloxy- or 1-acyloxypyridinium salts, was substituted by mercaptans in the absence of the corresponding sodium mercaptide to furnish a mixture of almost equal amounts of 2- and 3-alkylmercaptopyridines.[4] The purpose of this work was to explore the behavior of the three picoline N-oxides and some methylpyrazine N-oxides toward substitution by mercaptans in the presence of benzenesulfonyl chloride and acetic anhydride. Furthermore, it was of interest to ascertain if the methyl group exerted any directive influence on this ring substitution of the picoline N-oxides and, if under these conditions, the active methylene sites of 2- and 4-picoline N-oxides would be attacked.

The mercaptan chosen for this study was 1-propanethiol (in the formulas throughout the paper, R = *n*-Pr). The reaction of each picoline N-oxide produced a number of isomeric propylmercaptopicolines which were separated by column chromatography on alumina. A number of the thioethers isolated from these reactions were compared to specimens synthesized by unambiguous routes. When authentic specimens were not available, the isomers were identified by analysis and their nmr spectra. The nmr data are listed in Table I.[5,6]

When 2-picoline 1-oxide was treated with 1-propanethiol in the presence of benzenesulfonyl chloride, the five isomeric propylmercaptopicolines, I–V, were expected but only three of them were isolated, *viz.*, I, II, and III (eq 1). The major product consisted of 6-propylmercapto-2-picoline (I), which was identical with a sample prepared from the reaction of 6-chloro-2-picoline with sodium *n*-propylmercaptide.

The next largest fraction from the reaction consisted of isomer II. Identification was made readily from its nmr spectrum, which consisted of a doublet downfield assigned to H-6, which showed typical *meta* coupling (*para* coupling not being observed owing to the broadness of the bands), a doublet of doublets (H-4), and a doublet furthest upfield (H-3). Of all the possible isomers, I–V, II is the only one which possesses an α-proton (furthest downfield) which should show *meta* coupling (to a γ-proton).



(1)

The third and smallest fraction from this reaction was shown to be 4-propylmercapto-2-picoline (III), which was compared with a sample synthesized by literature methods.[7] Attempts to detect IV and V in the reaction mixture proved abortive. During the separation of the mixture on alumina, each small eluate was examined by its infrared spectrum and, when enough sample was present, also by its nmr spectrum. Thus, it should have been possible to detect IV, particularly since I and IV were the only disubstituted pyridines with three adjacent ring protons expected in the mixture and the spectra for I were available. Similarly, V (formed by active methylene substitution) would have been detected readily, particularly since its nmr spectrum exhibited an isolated CH_2 group (Table I). Hence, substitution in 2-picoline 1-oxide took place mainly at the α- and the adjacent β-positions, to a small degree at the γ-position, and apparently not at all at the β-position next to the methyl group.

When 3-picoline 1-oxide was subjected to this reaction, only three of the four (VI, VII, and VIII) possible

(1) This work constituted a part of the Ph.D. Dissertation by A. L. Hirsch, June 1965.

(2) Support by the National Science Foundation (Research Grant G-22191) for part of this work is gratefully acknowledged.

(3) L. Bauer and L. A. Gardella, *J. Org. Chem.*, **28**, 1323 (1963).

(4) L. Bauer and T. E. Dickerhofe, *ibid.*, **29**, 2183 (1964).

(5) The nmr spectra of pyridines are discussed by W. Brügel, *Z. Electrochem.*, **66**, 159 (1962).

(6) The nmr spectra of 2-amino-, 2-chloro-, and 2-nitropicolines, as well as long-range methyl to ring proton coupling, is presented by C. L. Bell, R. S. Egan, and L. Bauer, *J. Heterocyclic Chem.*, **2**, 420 (1965).

(7) The synthesis described by E. Profft and W. Rolle [*J. Prakt. Chem.*, **4**, 22 (1960)] consisted of displacing the nitro group in 4-nitro-2-picoline 1-oxide by *n*-propylmercaptide ion to form 4-propylmercapto-2-picoline 1-oxide, which was reduced by iron in acetic acid to form III.

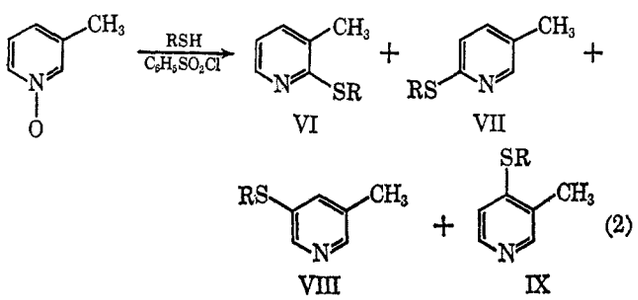
TABLE I

NMR PARAMETERS OF PROPYLMERCAPTOPICOLINES[a,b]

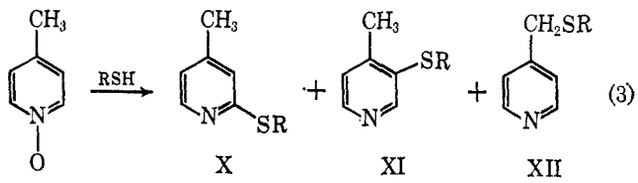
	Chemical shifts, ppm (δ) from TMS										Coupling constant of aromatic protons, cps							
Compd	CH_3	CH_2	CH_2S	$CH_{3(Ar)}$	$CH_{2(Ar)}$	H-2	H-3	H-4	H-5	H-6	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{2,4}$	$J_{3,5}$	$J_{4,6}$	$J_{2,5}$	$J_{3,6}$
I	0.97	1.63	3.14	2.37	...	...	6.85[c]	7.17	6.65[c]	...	7.2	6.5	...	...	1.0	...	...	...
II	0.93	1.52	2.80	2.43	...	...	6.97	7.53	...	8.49	7.4	...	...	...	...	2.1	...	...
III	0.97	1.58	2.86	2.42	...	...	6.95	...	6.84	8.29	...	...	4.5	...	1.5	...	...	0.7
IV	0.98	1.68	3.20	2.12	...	...	...	7.10[d]	6.70	8.25[d]	...	7.5	5.0	...	...	1.5	...	...
VII	0.97	1.65	3.14	2.10	...	...	6.92	7.15	...	8.19	7.5	...	...	...	...	2.1	...	0.9
VIII	0.93	1.53	2.85	2.16	...	8.19[e]	...	7.38	...	8.35[e]	...	...	...	1.4	...	1.8	...	...
IX	0.98	1.62	2.85	2.13	...	8.23	...	...	...	8.30	...	...	5.0	...	...	...	0.7	...
X	0.97	1.63	3.14	2.07	...	...	6.87[f]	...	6.62[f]	8.23	...	...	5.2	...	1.5	...	...	0.7
XI	0.97	1.55	2.85	2.28	...	8.55	...	...	7.01[g]	8.34	...	...	4.5	...	...	...	0.7	...
V	0.87	1.55	2.47	...	3.83	...	7.42	7.67	7.12	8.53	8.0	6.8	4.9	...	1.8	1.9	...	1.0
XII	0.85	1.50	2.35	...	3.63	8.53	7.25[h]	...	7.25[h]	8.53	...	...	4.4[i]	...	...	...	1.6	1.6

[a] The chemical shifts were obtained by first-order treatment. The signals for the ring protons[5,6] appeared in the following order, downfield from TMS: β (H-3, H-5), γ (H-4), and α (H-2, H-6) protons. [b] All spectra were determined neat. However, small coupling constants ($J_{2,5}$, $J_{3,6}$, and methyl to ring proton) were obtained more accurately from spectra in 20% $CDCl_3$ solution. [c] This assignment was made in the following manner. In the picolines, long-range coupling of the methyl groups to the *ortho* (*four* bonds) and *para* protons (six bonds) has been observed to be of the order of 0.5 cps, with the *ortho* coupling usually larger.[6] In 6-propylmercapto-2-picoline, two long-range couplings were found and assigned to $J_{CH_3,3} = 0.5$, $J_{CH_3,5} = 0.45$ cps. Thus, the β-proton adjacent to the methyl group appeared to be slightly more deshielded than the one next to the sulfide group. This conclusion is in agreement with the observation that the β-proton (H-3) in 5-propylmercapto-2-picoline (next to CH_3) is more deshielded than that of 2-propylmercapto-5-picoline (next to SR). [d] Long-range coupling of the methyl group to H-4 ($J = 0.75$ cps) and to H-6 ($J = 0.25$ cps) were observed. [e] Both signals were too broad to determine long-range CH_3 to ring-proton coupling constants. These assignments were arrived at by comparison with two model compounds in this series. In 4-propylmercapto-3-picoline the α-proton (H-2) adjacent to the methyl group is more shielded than the α-proton next to the sulfide group in 3-propylmercapto-4-picoline. The same relationship holds for the α-protons (H-6) next to the methyl and sulfide groups, respectively, in 2-propylmercapto-5- and 5-propylmercapto-2-picolines. [f] $J_{CH_3,3} = J_{CH_3,5} = 0.7$ cps. [g] $J_{CH_3,5} = 0.7$ cps. [h] $J_{CH_2Ar,3} = J_{CH_2Ar,5} = 0.5$ cps. [i] $J_{5,6} = J_{2,3}$.

ring-substituted thioethers were isolated in the ratio of approximately 3:1:2, respectively (eq 2). No substitution would have been expected in the relatively inactive β-methyl group. The major product was VI which was identified by comparison with an authentic sample obtained from the reaction of 3-methyl-2-pyridthione with *n*-propyl iodide. The other product of α substitution, VII, was also isolated and was found to be identical with a specimen made from 5-methyl-2-pyridthione and *n*-propyl iodide. The β-substituted product, 5-propylmercapto-3-picoline (VIII) was also isolated and its structure was established by its nmr spectrum, which consisted of two doublets downfield due to the α-protons and a complex multiplet upfield associated with H-4 (Table I). The remaining isomer, IX, could not be shown to be present. An authentic sample of IX was prepared from 4-nitro-3-picoline 1-oxide by the method used to synthesize III.[7] Thus it was apparent that entry of the sulfide group in 3-picoline 1-oxide occurred predominantly at the α- and β-positions. Interestingly enough, it appeared that position 2, being adjacent to the methyl group, which might appear less accessible to substitution than 6, was attacked more readily as evidenced by the ratio of VI:VII (almost 3:1).



Under identical conditions, 4-picoline 1-oxide was substituted in the ring only by 1-propanethiol in the presence of benzenesulfonyl chloride to give the two isomers X and XI in the ratio of 3:1 (eq 3).



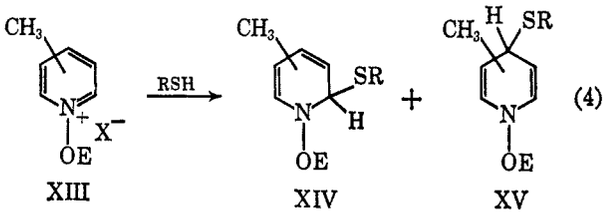
Whereas no active methylene substitution was observed in the last reaction, it was of interest to establish if such a substitution would occur when acetic anhydride was used as quaternizing agent.[4] The reaction of 4-picoline 1-oxide with acetic anhydride alone yielded primarily 4-pyridylmethyl acetate and some 3-acetoxy-4-picoline, thus involving mainly active methylene substitution.[8,9] It was hoped that, when the reaction of 4-picoline 1-oxide with 1-propanethiol is carried out in acetic anhydride, the highly nucleophilic mercaptide anion might attack the active methylene group in competition with the acetate anion. However, treatment of 4-picoline 1-oxide with 1-propanethiol in boiling acetic anhydride resulted in the entry of a sulfide group only at the ring positions to give X and XI in the ratio of 1:1. These results indicated that ring substitution again prevailed over that at the active methylene group also in acetic anhydride. These reactions demonstrate the difference in the mode of substitution under a variety of conditions: 4-picoline 1-oxide was attacked by 1-propanethiol mainly at the α-position in the presence of benzenesulfonyl chloride, at the α- and β-positions in acetic anhydride, in equal amounts, while 1-ethoxy-4-picolinium ethyl sulfate was

(8) (a) V. J. Traynelis and R. J. Martello, *J. Am. Chem. Soc.*, **82**, 2744 (1960); (b) S. Oae, Y. Kitaoka, and T. Kitoa, *Tetrahedron*, **20**, 2677 (1964).

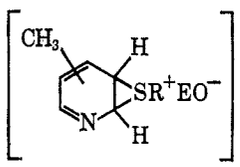
(9) In a recent report, P. W. Ford and J. M. Swan [*Australian J. Chem.*, **18**, 867(1965)] found that 2-picoline 1-oxide was substituted by acetic anhydride to give 2-pyridylmethyl acetate and 3- and 5-acetoxy-2-picolines in 66, 16, and 18% yield, respectively.

substituted by *n*-propylmercaptide ion predominantly at the β-ring position and the active methylene site.[3]

The mechanism postulated[4] for the substitution of pyridine N-oxide by mercaptan in the presence of acid halide and anhydrides (E^+X^-) can account for products of the cognate reactions of the picoline N-oxides. It was suggested that the N-oxide undergoes quaternization to form XIII (in the case of the picolines) which is attacked by mercaptide ion at the electrophilic sites to give XIV and XV (eq 4). Elimination of HOE from



XIII XIV XV

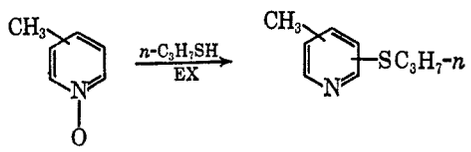


XVI

these dihydropyridines would give rise to the α- and γ-substituted pyridyl sulfides. The predominance of α over γ substitution (Table II) points to the greater

TABLE II

SUBSTITUTION OF PICOLINE 1-OXIDES BY MERCAPTANS

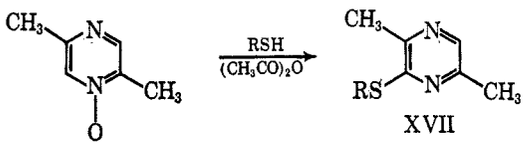


Position of CH_3 on ring	EX	Yield of sulfides, %	Position of entry of thio ether group with respect to the ring N— α	β	γ
None[a]	$C_6H_5SO_2Cl$	32	50	50	...
None[a]	$(CH_3CO)_2O$	67	61	39	...
2	$C_6H_5SO_2Cl$	9.4	52	42	6
3	$C_6H_5SO_2Cl$	7.2	67[b]	33	...
4	$C_6H_5SO_2Cl$	26	77	23	...
4	$(CH_3CO)_2O$	31	50	50	...

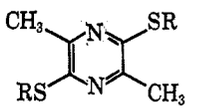
[a] Reference 4. [b] This represents both α-positions, the ratio at positions 2 and 6 being 3:1, respectively.

vulnerability of the α-position toward attack by mercaptans in this study. The mechanism suggested previously[4] to explain β substitution proposed that departure of OE from XIV or XV is accompanied by the migration of the sulfide group *via* an episulfonium ion (XVI), shown here for the one from the 1,2-dihydropyridine XIV. If β substitution is indeed the result of such a migration, this study suggests that it is most likely to take place from XIV on the following grounds. In the basic fraction from the reaction of 2-picoline 1-oxide with 1-propanethiol in the presence of benzenesulfonyl chloride, only *one* β-substituted product, *viz.*, 5-propylmercapto-2-picoline, was found. If migration took place from a 1,4-dihydro-2-picoline (see XV), one would have expected a mixture of 3- and 5-propylmercapto-2-picolines since it is not likely that the methyl group at C-2 (in XV) would offer sufficient steric hindrance to prevent migration of the sulfide group to C-3. The methyl group in 3-picoline 1-oxide apparently offers little hindrance to the substitution of the carbon adjacent to it; in fact, attack occurs preferentially at what seems like the less accessible site. A further experiment tends to substantiate that mercaptans attack 1-benzenesulfonyloxypyridinium salts preferentially at the α-position. With both α-positions blocked, 2,6-lutidine 1-oxide was not substituted by 1-propanethiol in the presence of benzenesulfonyl chloride under the general conditions of this reaction.[10] Thus, it appeared that in the absence of a free α-position, neither β nor γ substitution takes place in this particular substitution, although the γ-position does represent such a good electrophilic site.

An attempt to substitute some pyrazine N-oxides with 1-propanethiol in the presence of benzenesulfonyl chloride failed to introduce a propylmercapto group. However, when acetic anhydride was substituted for benzenesulfonyl chloride, ring protons α to the N-oxide function were substituted, at least in the two pyrazine N-oxides which were studied. When 2,5-dimethylpyrazine 1-oxide was treated with 1-propanethiol in boiling acetic anhydride, the thioether XVII was isolated, whose nmr spectrum clearly indicated two methyl groups and one ring proton, thus elimi-



XVII



XVIII

nating active methylene substitution. Similarly, 2,5-dimethylpyrazine 1,4-dioxide reacted with the same reagents to furnish as the major product the bisthioether, XVIII. It is not clearly understood at present why acetic anhydride was instrumental in effecting this substitution in the pyrazine N-oxides which failed with benzenesulfonyl chloride.

Experimental Section[11]

Materials.—We gratefully acknowledge the generous gifts of N-oxides from Reilly Tar and Chemical Co., those of 1-propanethiol from Pennsalt Chemical Co. and Phillips Petroleum Co. Activated alumina used for chromatography was

(10) The possibility that 2,6-lutidine 1-oxide is too hindered to react initially with benzenesulfonyl chloride to form 1-benzenesulfonyloxy-2,6-lutidinium chloride is not likely. It has been reported by E. Matsumura, T. Hirooka, and K. Imagawa [*Nippon Kagaku Zasshi*, **82**, 616 (1961)] that 2,6-lutidine 1-oxide reacts with *p*-toluenesulfonyl chloride to give 2-chloromethyl-6-picoline (72%), presumably *via* 1-(*p*-toluenesulfonyloxy)-2,6-lutidinium chloride.

(11) Melting points and boiling points are uncorrected. Microanalyses for nitrogen were obtained by Mr. Leo Horner in this department by the use of a Coleman nitrogen analyzer, Model 29, and others from Micro-Tech Laboratories, Inc., Skokie, Ill., and Dr. Kurt Eder, Geneva, Switzerland. All infrared spectra were determined as liquid films between salt plates by means of the Perkin-Elmer spectrophotometer, Model 337. Nmr spectra were recorded by means of the Varian A-60 spectrometer, signals mentioned being downfield from tetramethylsilane (TMS) as internal standard. The number of protons assigned to each area was obtained from the integration curve and agreed with the assignments made.

purchased from Alcoa (Grade F-20). Petroleum ether (Mallinckrodt) refers to the fraction of bp 30–60°. Sodium hydride (Metal Hydrides) was handled as a 53% suspension in mineral oil.

Synthesis of Reference Compounds. 4-Propylmercapto-3-picoline.—Sodium *n*-propylmercaptide was prepared by adding 1-propanethiol (10.8 ml, 0.12 mole) slowly to a suspension of sodium hydride (2.64 g, 0.12 mole) in N,N-dimethylformamide (125 ml). The resultant dispersion was added dropwise (1 hr) to a suspension of 4-nitro-3-picoline 1-oxide[12] (12.0 g, 0.08 mole) in N,N-dimethylformamide (50 ml). The mixture was heated at 100° for an additional hour, cooled, acidified with 10% hydrochloric acid and evaporated to dryness *in vacuo*. The residue was dissolved in acetic acid (30 ml) and iron powder (8 g) was added to it. The mixture was heated on the steam bath for 2 hr, cooled, made basic with 10% sodium hydroxide, and steam distilled. The organic layer of the steam distillate was extracted into methylene chloride and distilled. The product (7.81 g, 60%) boiled at 90–91° at 0.4 mm, $n^{25}D$ 1.5589. Its infrared absorptions bands were found at 3090 (w), 3025 (m), 2960 (vs), 2940 (s), 2875 (m), 1580 (vs), 1545 (w), 1475 (s), 1450 (s), 1400 (m), 1380 (w), 1295 (m), 1245 (w), 1202 (m), 1100 (s), 1065 (w), 1040 (vw), 996 (m), 900 (w), 815 (vs), 750 (w), 732 (m), and 700 (s) cm^{-1}.

Anal. Calcd for $C_9H_{13}NS$: C, 64.61; H, 7.83; N, 8.38. Found: C, 64.77; H, 7.97; N, 8.47.

4-Propylmercapto-2-picoline.—The thioether was prepared[7] in 21% yield from 4-nitro-2-picoline 1-oxide[13] as described above for 4-propylmercapto-3-picoline. It boiled at 83–84° at 0.6 mm, $n^{25}D$ 1.5512, lit.[7] bp 131° (15 mm). Its infrared spectrum possessed the following bands: 3050 (w), 2975 (vs), 2940 (s), 2880 (s), 1590 (vs), 1549 (m), 1470 (s), 1390 (m), 1290 (m), 1230 (m), 1109 (s), 1090 (sh), 1042 (w-b), 990 (w), 880 (sh), 869 (s), 815 (s), 750 (w), and 705 (s) cm^{-1}.

2-Propylmercapto-3-picoline.—A solution of 3-methyl-2-pyridthione[6] (1.25 g, 0.01 mole) in tetrahydrofuran was treated first with sodium hydride (0.26 g, 0.01 mole), then dropwise with 1-iodopropane (1.7 g, 0.01 mole), and the mixture was heated under reflux for 1 hr. Hydrochloric acid (10%, 20 ml) was added and the volume was reduced to one-third *in vacuo*, and the residue was extracted with benzene–ether (1:1, two 50-ml portions). The pH was adjusted to 8 with 10% sodium hydroxide solution and the base was extracted into methylene chloride. Distillation of this extract yielded the product (1.2 g, 72% yield), bp 60–61° (0.3 mm), $n^{25}D$ 1.5535. Its infrared spectrum showed the following bands: 3040 (w), 2960 (s), 2925 (sh), 2860 (w), 1580 (s), 1565 (sh), 1460 and 1440 (m), 1390 (vs), 1290 (w), 1240 (w), 1194 (m), 1135 (m), 1087 (s), 1035 (w), 988 (m), 819 (m), 780 (s), 740 (m), and 675 (m) cm^{-1}.

Anal. Found: C, 64.77; H, 7.96; N, 8.23.

2-Propylmercapto-5-picoline.—The reaction of 5-methyl-2-pyridthione[6] (1.25 g, 0.01 mole) with 1-iodopropane and sodium hydride as described directly above gave the **thioether** (0.84 g, 60%), bp 68–70° (1.3 mm), $n^{25}D$ 1.5505. Its infrared spectrum exhibited the following bands: 2975 (s), 2940 (m), 2890 (m), 1600 (s), 1560 (w), 1470 (vs), 1375 (s), 1295 (w), 1272 (m), 1145 (s), 1112 (vs), 1025 (m), 890 (vw), 818 (s), and 733 (w) cm^{-1}.

Anal. Found: C, 65.08; H, 7.90; N, 8.09.

2-Propylmercapto-6-picoline.—1-Propanethiol (4.5 ml, 0.05 mole) was added dropwise to a suspension of sodium hydride (1.2 g, 0.05 mole) in freshly distilled N,N-dimethylformamide (50 ml). To this mixture was added 6-chloro-2-picoline (6.35 g, 0.05 mole) and the mixture was heated under reflux for 2 hr. The product was isolated as described for 4-propylmercapto-3-picoline (above) and distilled at 72–74° (0.5 mm), $n^{25}D$ 1.5435. It weighed 2.1 g (25%). Its infrared bands were found at 3060 (w), 2970 (vs), 2940 (m), 2870 (m), 1575 (vs), 1449 (vs), 1380 (m), 1348 (vw), 1290 (w), 1258 and 1240 (w), 1160 (vs), 1148 (sh), 1088 (w), 1035 (vw), 1000 (w), 975 (w), 890 (sh), 872 (s), 775 (vs), 730 (m), and 679 (m) cm^{-1}.

Anal. Found: C, 64.64; H, 7.85; N, 8.49.

Reaction of 2-Picoline 1-Oxide with 1-Propanethiol in the Presence of Benzenesulfonyl Chloride.—Benzenesulfonyl chloride (128 ml, 1 mole) was added dropwise (0.25 hr) to an ice-cold well-stirred suspension of 2-picoline 1-oxide (54.5 g, 0.5 mole) in 1-propanethiol (250 ml). The mixture was then heated under reflux on a steam bath for 2 hr, after which most of the thiol was distilled. To the residue was added water and then the acid solution (pH 1–2) was extracted with benzene–ether (1:1; four 100-ml portions). The aqueous layer was made basic by means of 2 *N* sodium hydroxide solution and extracted by methylene chloride (five 100-ml portions). Distillation of this extract furnished a mixture (17.1 g), bp 78–95° (0.2 mm).

A portion of the distillate (5 g) was placed on alumina (100 g) and eluted in 50-ml portions of solvents. The elution of the column was followed by examining the infrared spectra of the fractions, and identical fractions were combined and distilled and identified by their nmr spectra when compared with those of the reference compounds. The following products were obtained. 6-Propylmercapto-2-picoline (1.2 g) was eluted first by petroleum ether (500 ml), followed by 5-propylmercapto-2-picoline (0.97 g), eluted by 1:1 petroleum ether–benzene (350 ml) and benzene (50 ml), and then by 4-propylmercapto-2-picoline (0.13 g) by 1:1 benzene–ether (200 ml) and ether (200 ml). Further elution by methylene chloride and then ethanol gave mainly starting N-oxide.

5-Propylmercapto-2-picoline (identified by its nmr spectrum, see Discussion) was distilled: bp 70–71° (0.5 mm), $n^{25}D$ 1.5452. Its infrared bands were at 3050 (w), 3000 (sh), 2960 (vs), 2920 (m) 2870 (m), 1575 (s), 1550 (w), 1470 (vs, b), 1375 and 1355 (m), 1291 (m), 1238 (m), 1140 (m), 1109 (m), 1020 (s), 895 (w), 825 (s), and 729 (m) cm^{-1}.

Anal. Found: C, 64.95; H, 8.15; N, 8.05.

Reaction of 3-Picoline 1-Oxide with 1-Propanethiol in the Presence of Benzenesulfonyl Chloride.—A similar reaction of 3-picoline 1-oxide (54.5 g, 0.5 mole) afforded after work-up a mixture (15.7 g), bp 87–105° (mainly between 87 and 97°) at 1.2 mm.

Chromatography of a portion of this distillate (5.22 g) on alumina (100 g) furnished the following pure thio ethers. 2-Propylmercapto-3-picoline (0.96 g) was eluted by petroleum ether (325 ml), then 2-propylmercapto-5-picoline (0.35 g) was eluted with petroleum ether (200 ml) and benzene–petroleum ether (1:1, 200 ml), followed by 5-propylmercapto-3-picoline (0.69 g) eluted by benzene (225 ml) and benzene–ether (1:1, 200 ml). The last compound was identified by its nmr spectrum (see Discussion). It was distilled for analysis: bp 70–72° (0.2 mm), $n^{25}D$ 1.5509. Its infrared bands were at 3020 (m), 2960 (vs), 2925 (s), 2870 (s), 1580 (s), 1560 (sh), 1455 (s), 1420 (vs), 1380 (m), 1310 (w), 1290 (m), 1230 (s), 1162 (m), 1105 (vs), 1025 (m), 880 (s), 858 (s), 783 (w), 706 (vs), and 679 (m) cm^{-1}.

Anal. Found: C, 65.10; H, 7.85; N, 8.49.

Reaction of 4-Picoline 1-Oxide with 1-Propanethiol. A. In the Presence of Benzenesulfonyl Chloride.—A cognate reaction of 4-picoline 1-oxide (0.5 mole) as described above yielded a mixture of thio ethers (25.2 g), bp 76–86° (0.3 mm).

Chromatography of 5.0 g of this distillate on alumina (100 g) gave on elution with petroleum ether (800 ml) 2-propylmercapto-4-picoline (3.3 g), bp 80–81° (0.2 mm), $n^{25}D$ 1.5495, identical with that described in the literature.[3] Further elution with benzene–ether (1:1, 400 ml) and ether (200 ml) produced 3-propylmercapto-4-picoline (1.0 g), bp 79–80° (0.5 mm), $n^{25}D$ 1.5510, identical with the sample described previously.[3]

B. In Acetic Anhydride.—A solution of 4-picoline 1-oxide (10.9 g, 0.1 mole) and 1-propanethiol (22.8 g, 0.2 mole) in acetic anhydride (100 ml) was heated at 140° for 2 hr and then concentrated at 100° and 20 mm. The residue was diluted with hydrochloric acid (1:5, 60 ml) and extracted with 1:1 benzene–ether (two 100-ml portions). The acid aqueous solution was made basic with sodium hydroxide pellets and boiled under reflux for 1 hr,[14] cooled, and extracted with methylene chloride (four 100-ml portions). Distillation gave a fraction (9.39 g), bp 80–120° (mainly between 100 and 110°) at 1.5 mm. A 5-g, portion of this distillate was chromatographed on alumina (100 g) and there was eluted by petroleum ether (700 ml) 2-

(12) E. C. Taylor and J. Crovetti, "Organic Syntheses," Coll. Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1963, p 654.

(13) Prepared in 78% yield from 2-picoline 1-oxide by the method described for the nitration of 3-picoline 1-oxide.[12] Its melting point, 154–155°, compared with that reported by H. J. den Hertog, C. R. Kolder, and W. P. Combé [*Rec. Trav. Chim.*, **70**, 591 (1951)], who nitrated 2-picoline 1-oxide phthalate.

(14) This step was included to hydrolyze esters formed from the reaction of 4-picoline 1-oxide and acetic anhydride (see ref 8 and 9). It was found that the chromatographic separation of the sulfides proceeded more satisfactorily. Such a hydrolysis and subsequent extraction of the basic medium would remove the amphoteric 4-methyl-3-pyridinol and would separate it from 4-pyridinemethanol. The latter, being an alcohol, would be absorbed strongly on the alumina.

propylmercapto-4-picoline (1.35 g), bp 83–84° (1.2 mm) [lit.[3] bp 67° (2 mm)], and then by benzene (500 ml), 3-propylmercapto-4-picoline (1.4 g), bp 78–79° (0.5 mm) [lit.[3] bp 139–140° (21 mm)].

2,5-Dimethyl-3-propylmercaptopyrazine.—A solution of 2,5-dimethylpyrazine 1-oxide[15] (3.1 g, 0.025 mole) and 1-propanethiol (5.7 g, 0.075 mole) in acetic anhydride (40 ml) was heated under reflux for 2 hr and then distilled. The fraction, bp 87–90° (0.1 mm) (2.7 g), was chromatographed on alumina (60 g), and the **sulfide** (1.23 g, 27%) was eluted by petroleum ether (350 ml) and benzene (200 ml), bp 73–75° (0.2 mm), $n^{25}D$ 1.5436. The nmr spectrum (neat) showed the pyrazine proton at δ 7.83, the two methyl groups as a singlet (δ 2.38, shoulder at δ 2.35), the propylmercapto group with the CH_2S at δ 3.10 (triplet), $C-CH_2-C$ as a multiplet at δ 1.64, and the CH_3 at δ 1.02 (triplet).

(15) C. F. Koelsch and W. H. Gumprecht, *J. Org. Chem.*, **23**, 1603 (1958).

Anal. Calcd for $C_9H_{14}N_2S$: C, 59.29; H, 7.74; N, 15.37. Found: C, 59.68; H, 7.81; N, 15.15.

2,5-Dimethyl-3,6-dipropylmercaptopyrazine.—A solution of 2,5-dimethylpyrazine 1,4-dioxide[16] (7.0 g, 0.05 mole) and 1-propanethiol (18 ml, 0.2 mole) in acetic anhydride (80 ml) was allowed to react as shown above for the mono-N-oxide to give a fraction (10 g), bp 121–126° (0.5 mm). Chromatography on 200 g of alumina gave the **sulfide** as the major fraction (2.50 g, 20%), mp 34°, being eluted by petroleum ether (400 ml), which could be crystallized from acetonitrile–ethanol (9:1), with poor recovery: mp 34–35°. Its nmr spectrum was devoid of aromatic protons and just exhibited resonances due to the aromatic CH_3 and $S-CH_2CH_2CH_3$ group.

Anal. Calcd for $C_{12}H_{20}N_2S_2$: C, 56.20; H, 7.86; N, 10.93. Found: C, 56.20; H, 8.08; N, 10.95.

(16) G. T. Newbold and F. S. Spring, *J. Chem. Soc.*, 1183 (1947).

The Reactions of Metallocenes with Electron Acceptors[1a]

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The reaction products of ferrocene, cobaltocene, and bis(tetrahydroindenyl)iron with 2,3-dichloro-5,6-dicyanoquinone (DDQ) and tetracyanoethylene (TCNE) have been isolated and their physical properties, including infrared spectra, visible spectra, and electrical resistivities, have been determined. The equilibrium constants for the reaction, metallocene + TCNE = metallocinium + $TCNE\cdot^-$, have been measured in various solvents. The relationship between the oxidation–reduction potentials of the metallocenes and the properties of the products is discussed.

The recent interest in metallocene complexes has focused attention on the structure of these materials. In general, the structure has been formulated either in terms of π complexes or in terms of metallocinium salts. In the former case, the metallocene is considered to be a donor interacting with an acceptor, whereas in the second case the complete transfer of an electron from the donor to the acceptor gives rise to an ionic compound.[2]

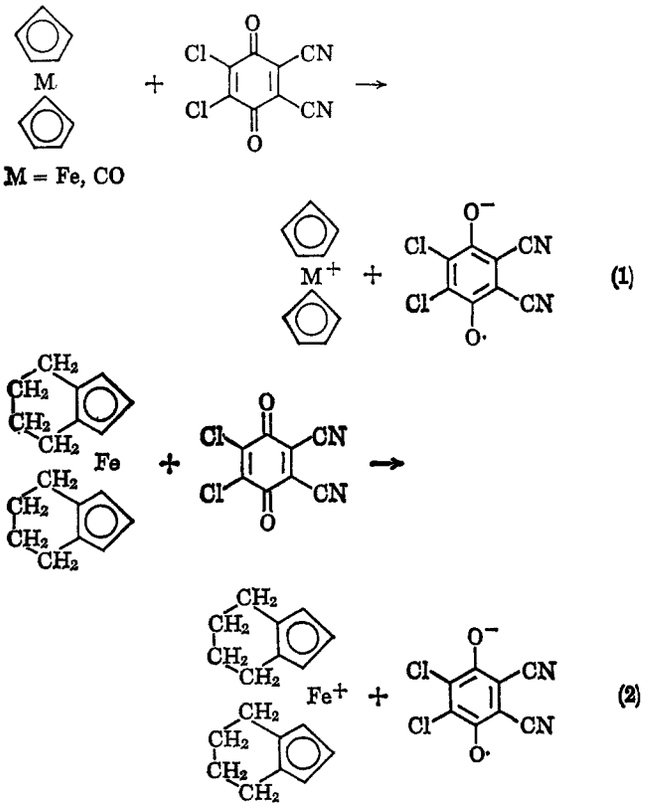
Our interest in the electrical properties of π complexes has prompted the synthesis of a number of metallocinium compounds by the reaction of ferrocene, cobaltocene, and bis(tetrahydroindenyl)iron[3] with tetracyanoethylene (TCNE) and 2,3-dichloro-5,6-dicyanoquinone (DDQ). We wish to report some of the physical properties of these compounds and some observations on their structure.

Results

Complexes with 2,3-Dichloro-5,6-dicyanoquinone.—Ferrocene, bis(tetrahydroindenyl)iron, and cobaltocene react with DDQ in benzene to give black crystalline products which are essentially insoluble in nonpolar solvents, but which may be recrystallized from polar solvents such as acetonitrile. The products give satisfactory analyses for 1:1 ratios of metallocene and quinone.

The infrared spectra of the products are noticeably different from the spectra of the components. The carbonyl band of DDQ at 1680 cm^{-1} is absent as are characteristic bands of the metallocenes. Several similarities among the spectra of the three complexes are noted. In particular, the absorption at 2230 cm^{-1} owing to the nitrile group is greatly enhanced, and in all three compounds bands of similar intensity appear near 1600–1580, 1230, 1190, 1050, and 780 cm^{-1}.

These results suggest that the reaction should be formulated as indicated in eq 1 and 2. The pertinent



(1) (a) This work was supported by Lockheed Independent Research Fund. (b) To whom inquiries should be sent.

(2) A complete theory of charge-transfer complexes has been proposed by R. S. Mulliken, *J. Am. Chem. Soc.*, **74**, 811 (1952).

(3) J. H. Osiecki, C. J. Hoffman, and D. P. Hollis, *J. Organometal. Chem.* (Amsterdam), **3**, 107 (1965).