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A series of pyridylalkylthiols and their derivatives have been prepared as potential radiation-protection agents.

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The amino acid cysteine (4) and 2-aminoethanethiol (5) have been shown to increase the life span of mice when they were exposed to lethal doses of X- or gamma radiation. Since these pioneering observations, a great variety of organic compounds, primarily containing nitrogen and sulfur, have been prepared and screened as radiation-protection agents with varying degrees of success (6,7,8,9,10,11,12,13,14,15).

The compounds prepared in this investigation are listed in Tables Ia, Ib, Ic, and IIa, IIb together with the supporting analytical and spectral data. The balance of the compounds prepared are described in the experimental.

Some of the compounds prepared have been screened as antiradiation agents (16). 3-(3-Pyridyl)-1-propanethiol hydrochloride produced no protection at 51-150 mg./kg. 6-Methyl-2-(2-pyridylethyl)isothiuronium dihydrobromide 1-oxide gave no protection at 151-350 mg./kg. 5-Ethyl-2-(2-pyridylethyl)isothiuronium dihydrobromide 1-oxide did not protect at 50 mg./kg. 6-Methyl-2-(2-pyridyl)ethyl Bunte salt exhibited *some* protection at 351-750 mg./kg. 4,6-Dimethyl-2-(2-pyridyl)ethyl Bunte salt showed *some* protection at 351-750 mg./kg. 2-(2-Pyridyl)ethyl Bunte salt exhibited *some* protection at 351-750 mg./kg. 2-(4-Pyridyl)ethanethiol 1-oxide gave significant activity at mid-lethal doses although no activity was shown at 51-150 mg./kg. 3-(4-Pyridyl)propanethiol hydrochloride gave no protection at 50 mg./kg. 3-(4-Pyridyl)propanethiol 1-oxide showed no protection at 51-150 mg./kg. 3-(3-Pyridyl)propanethiol 1-oxide gave no protection at 51-150 mg./kg.

EXPERIMENTAL (17)

Preparation of the Pyridylalkyl Chlorides (Table I).

The following procedure illustrates the preparation of pyridylalkyl chlorides listed in Tables Ia,b,c.

To 2-(5-ethyl-2-pyridyl)-1-ethanol (30.2 g., 0.2 mole) in 100 ml. of dry chloroform was added thionyl chloride (35.3 g., 0.3 mole) in 50 ml. of dry chloroform with stirring in an ice bath. The reaction mixture was stirred one hour at room temperature and one hour at 60°. The chloroform and excess thionyl chloride were removed under reduced pressure and water was added to the residue. The residue was neutralized with concentrated ammonium hydroxide and extracted with chloroform and the chloroform solution was dried (sodium sulfate) and the chloroform evaporated. The brown liquid was distilled at 84-85° at 0.15 mm Hg to give a colorless liquid, 2-(β-chloroethyl)-5-ethylpyridine. A picrate was prepared for analysis (Table Ia).

2-(5-Ethyl-2-pyridyl)-1-ethanethiol.

2-(5-Ethyl-2-pyridyl)-1-chloroethane (15 g., 0.0885 mole) in 50 ml. of absolute ethanol and potassium hydrogen sulfide (prepared by allowing hydrogen sulfide to saturate an ice cold solution containing 10 g. (0.18 mole) of potassium hydroxide dissolved in 10 ml. of water and 50 ml. of ethanol) were heated at 60-70° for three hours. Upon cooling the potassium chloride was removed by filtration and the solvents removed *in vacuo*. To the residue was added 10 ml. of water saturated with ammonium chloride and extracted with chloroform. The chloroform solution was dried (sodium sulfate) and the chloroform removed by distillation. Fourteen g. of a brown oil was obtained which gave 7.5 g. (51%) of a colorless liquid, b.p. 102-104° at 0.25 mm Hg upon distillation. A picrate was prepared, yellow prisms from methanol, m.p. 106°.

Anal. Calcd. for $C_9H_{13}NS \cdot C_6H_3N_3O_7$: C, 45.5; H, 4.0; N, 14.2. Found: C, 45.2; H, 4.0; N, 14.1.

2-(2,4-Dinitrophenylthioethyl)-5-ethylpyridine.

To 2-(5-ethyl-2-pyridyl)-1-ethanethiol (1.7 g., 0.01 mole) and 0.4 g. of sodium hydroxide in 30 ml. of 80% ethanol was added 2.0 g. (0.01 mole) of 2,4-dinitrochlorobenzene in 10 ml. of ethanol and the mixture heated on the steam bath for 10 minutes. The hot solution was quickly filtered and the product crystallized as yellow needles on cooling. On crystallization from ethanol, 2.5 g. of product, m.p. 93-94° was obtained.

Anal. Calcd. for $C_{15}H_{15}N_3O_4S$: C, 54.1; H, 4.5; N, 12.6. Found: C, 53.9; H, 4.7; N, 12.5.

The pyridylalkylthiols and the 2,4-dinitrophenylthioalkylpyridines were all prepared in an analogous manner to that described above. The essential details are described below.

2-(2-Pyridyl)-1-ethanethiol.

From 35 g. (0.248 mole) of 2-(2-chloroethyl)pyridine, 17.5 g. (51%) of a colorless oil, b.p. 77-78° at 0.15 mm Hg, $n_D^{26.5}$ = 1.5729, was obtained after two vacuum distillations. The picrate, yellow prisms from methanol had m.p. 163-164°.

Anal. Calcd. for $C_7H_9NS \cdot C_6H_3N_3O_7$: C, 42.4; H, 3.3; N, 15.2. Found: C, 42.6; H, 3.1; N, 15.4.

The styphnate, yellow needles from methanol had m.p. 156°.

Anal. Calcd. for $C_7H_9NS \cdot C_6H_3N_3O_8$: C, 40.6; H, 3.1; N, 14.6. Found: C, 41.0; H, 2.9; N, 15.0.

2-[2-(2,4-Dinitrophenylthio)ethyl]pyridine.

From 1.4 g. (0.01 mole) of 2-(2-pyridyl)ethanethiol there was obtained 2.5 g. (82%) of product after two recrystallizations from ethanol, m.p. 122°; pmr (DMSO-d_6): δ 3.18 (t, J = 6 Hz), 3.56 (t, J = 6 Hz), 7.2-8.0 (m, 4H), 8.34-8.60 (m, 2H), 8.82 (d, J = 2 Hz).

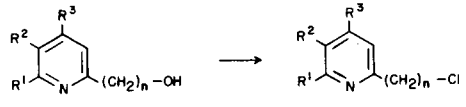
Anal. Calcd. for $C_{13}H_{11}N_3O_4S$: C, 51.1; H, 3.6; N, 13.8. Found: C, 51.2; H, 3.3; N, 14.1.

3-(3-Pyridyl)-1-propanethiol.

From 31.1 g. (0.2 mole) of 3-(3-chloro-1-propyl)pyridine, there was obtained 14.6 g. (48%) of a colorless oil, b.p. 92-99° at 0.15 mm Hg. The picrate, yellow prisms from methanol had m.p. 113-114°.

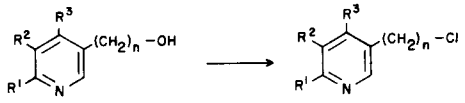
Anal. Calcd. for $C_8H_{11}NS \cdot C_6H_3N_3O_7$: C, 44.0; H, 3.7; N,

Table Ia



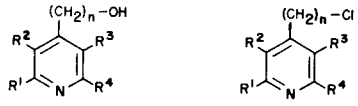
Compound No.	R^1	R^2	R^3	n	% Yield	B.p. °C/mm	M.p. °C	Recrystallization solvent	Formula	Analyses C Calcd.	C Found	H Calcd.	H Found	N Calcd.	N Found
1	H	Ethyl	H	2	86	84-85/0.15			$C_9H_{12}ClN$						
1-picrate	H	Ethyl	H	2			125	Methanol	$C_9H_{12}ClN \cdot C_6H_3N_3O_7$	45.2	45.2	3.8	3.8	14.0	14.1
2	H	H	H	2	76	68-72/0.25			C_7H_8ClN						
2-picrate	H	H	H	2			119-120	Methanol	$C_7H_8ClN \cdot C_6H_3N_3O_7$	42.1	42.1	3.0	3.2	15.1	14.9
3	Methyl	H	Methyl	2	86	78/0.25			$C_9H_{12}ClN$						
3-picrate	Methyl	H	Methyl	2			112-114	Methanol	$C_9H_{12}ClN \cdot C_6H_3N_3O_7$	45.2	45.1	3.8	3.9	14.1	14.5

Table Ib



4	H	H	H	3	80	95-98/0.3			$C_8H_{10}ClN$						
4-picrate	H	H	H	3			137	Methanol	$C_8H_{10}ClN \cdot C_6H_3N_3O_7$	43.7	43.6	3.4	3.3	14.6	14.3

Table Ic



	R^1	R^2	R^3	R^4											
5	H	H	H	H	2	96			C_7H_8ClN						
5-picrate	H	H	H	H	2		126.5	Methanol	$C_7H_8ClN \cdot C_6H_3N_3O_7$	42.1	42.2	3.0	3.0	15.1	15.3
6	H	H	H	H	3	85	52/0.2								
6-picrate	H	H	H	H	3		130	Methanol	$C_8H_{10}ClN \cdot C_6H_3N_3O_7$	43.8	43.6	3.4	3.6		
7	H	H	H	H	3		142	Ethanol-ethyl acetate	$C_8H_{10}ClN \cdot HCl$	50.0	49.7	5.8	5.4		

14.7. Found: C, 43.6; H, 3.5; N, 14.7.

The hygroscopic 3-(3-pyridyl)-1-propanethiol hydrochloride was obtained from ethereal hydrogen chloride.

Anal. Calcd. for $C_8H_{11}NS \cdot HCl$: C, 50.7; H, 6.4; N, 7.4. Found: C, 50.7; H, 5.9; N, 7.0.

2-(4,6-Dimethyl-2-pyridyl)-1-ethanethiol.

This compound (b.p. 76-79° at 0.2 mm Hg) was obtained in 52% yield (7.4 g.) from 14.5 g. (0.085 mole) of 2-(2-chloroethyl)-4,6-dimethylpyridine. 2-(4,6-Dimethyl-2-pyridyl)-1-ethanethiol (1.7 g., 0.01 mole) gave 3.2 g. (95%) of yellow needles (from ethanol) of 2-[2-(2,4-dinitrophenylthio)ethyl]-4,6-dimethylpyridine, m.p. 123°; pmr (DMSO-d_6): δ 2.26 (s), 2.40 (s), 3.08 (t, J = 6.0 Hz), 3.56 (t, J = 6.0 Hz), 6.90 (broad s), 7.90 (d, J = 8.0 Hz), 8.44 (dd, J = 8.0 Hz and J = 2.0 Hz), 8.80 (d, J = 2.0 Hz).

Anal. Calcd. for $C_{15}H_{15}N_3O_4S$: C, 54.1; H, 4.5; N, 12.6. Found: C, 54.2; H, 4.6; N, 12.5.

4-(2,4-Dinitrophenylthioethyl)pyridine.

From 1.4 g. (0.01 mole) of 2-(4-pyridyl)-1-ethanethiol, 2.8 g. (92%) of yellow needles from ethanol, m.p. 134-135° was obtained; pmr (DMSO-d_6): δ 3.10 (t, J = 6.0 Hz), 3.56 (t, J = 6.0 Hz), 6.14 (d, J = 4.0 Hz, 2H), 7.92 (d, J = 9.0 Hz), 8.72-9.12 (m, 3H), 8.88 (d, J = 2.0 Hz).

Anal. Calcd. for $C_{13}H_{11}N_3O_4S$: C, 51.1; H, 3.6; N, 13.8. Found: C, 51.5; H, 3.5; N, 14.0.

2-(4-Pyridyl)-1-ethanethiol.

From 26 g. (0.18 mole) of 4-(2-chloroethyl)pyridine, there was obtained 12.3 g. (48%) of a yellow oil, b.p. 84-86° at 0.4 mm Hg. The picrate, yellow needles from methanol had m.p. 122°.

Anal. Calcd. for $C_7H_9NS \cdot C_6H_3N_3O_7$: C, 42.4; H, 3.3; N, 15.2. Found: C, 42.5; H, 3.4; N, 15.4.

The hydrochloride was crystallized from methanol-ethyl acetate, m.p. 235° dec.; pmr (DMSO-d_6): δ 3.30 (m, 4H), 8.14 (d, J = 6.0 Hz), 8.98 (d, J = 6.0 Hz).

Anal. Calcd. for $C_7H_9NS \cdot HCl$: C, 47.9; H, 5.7. Found: C, 47.9; H, 5.5.

2-(6-Methyl-2-pyridyl)-1-ethanethiol.

From 13.0 g. (0.084 mole) of crude 2-(2-chloroethyl)-6-methylpyridine, 5.1 g. (39%) of product, b.p. 66-68° at 0.4 mm Hg was obtained. This compound was characterized as 2-(2,4-dinitrophenylthioethyl)-6-methylpyridine (see below). In addition the monosulfide was obtained as an alkali insoluble oil (6.1 g., 47%). The hydrochloride was crystallized from methanol-ethyl acetate, m.p. 221-223°.

Anal. Calcd. for $C_{16}H_{20}N_2S \cdot HCl$: C, 55.7; H, 6.4. Found: C, 55.5; H, 6.3.

2-(2,4-Dinitrophenylthioethyl)-6-methylpyridine.

A yield of 1.9 g. of product, m.p. 91°, yellow prisms from ethanol was obtained from 1.0 g. of 2-(6-methyl-2-pyridyl)-1-ethanethiol.

Anal. Calcd. for $C_{14}H_{13}N_3O_4S$: C, 52.7; H, 4.1. Found: C, 52.3; H, 3.8.

3-(4-Pyridyl)-1-propanethiol.

From 25 g. (0.16 mole) of 4-(3-chloropropyl)pyridine, there was obtained 12.0 g. (49%) of product as a colorless oil, b.p. 84-85° at 0.25 mm Hg and 6.5 g. (26%) of the monosulfide, b.p. 180-200° at 0.25 mm Hg.

The picrate of 3-(4-pyridyl)-1-propanethiol had m.p. 108-109°, yellow leaflets from methanol.

Anal. Calcd. for $C_8H_{11}NS \cdot C_6H_3N_3O_7$: C, 44.0; H, 3.7. Found: C, 44.1; H, 3.2.

The hydrochloride of 3-(4-pyridyl)-1-propanethiol from methanol-ethyl acetate had m.p. 122°.

Anal. Calcd. for $C_8H_{11}NS \cdot HCl$: C, 50.7; H, 6.4; N, 7.4. Found: C, 50.6; H, 6.2; N, 7.3.

The dipicrate of the monosulfide had m.p. 168° from acetone.

Anal. Calcd. for $C_{16}H_{20}N_2S \cdot 2C_6H_3N_3O_7$: C, 46.0; H, 3.6. Found: C, 45.6; H, 3.5.

4-[3-(2,4-Dinitrophenylthio)propyl]pyridine.

From 1.0 g. of 3-(4-pyridyl)-1-propanethiol, there was obtained 1.3 g. of product, m.p. 103° from ethanol; pmr (DMSO-d_6): δ 2.08 (quintet, J = 8.0 Hz), 2.88 (t, J = 8.0 Hz), 3.26 (t, J = 8.0 Hz), 7.24-7.36 (m, 2H), 7.84 (d, J = 8.0 Hz), 8.32-8.66 (m, 3H), 8.86 (d, J = 2.0 Hz).

Anal. Calcd. for $C_{14}H_{13}N_3O_4S$: C, 52.7; H, 4.1. Found: C, 52.5; H, 4.1.

1-(2-Pyridyl)-3-tosyloxypropane.

A mixture containing 14.0 g. (0.102 mole) of 3-(2-pyridyl)-1-propanol and 19.0 g. (0.1 mole) of *p*-toluenesulfonyl chloride in 32 ml. of pyridine was allowed to stand at room temperature for five days. The solid pyridine hydrochloride which separated was removed by filtration and the filtrate was concentrated *in vacuo*. The residue solidified after treatment with sodium carbonate and extracted with chloroform. The chloroform was evaporated and the solid residue was crystallized from methanol-ethyl acetate, giving 22 g. (75%) of product, m.p. 125-128°. An analytical sample was prepared by recrystallization from methanol-ethyl acetate, colorless needles, m.p. 128-130°.

Anal. Calcd. for $C_{15}H_{17}NO_3S$: C, 61.8; H, 5.9. Found: C, 61.6; H, 5.6.

The Synthesis of Pyridylalkylthiol *N*-Oxides and Related Compounds.

The detailed preparation of this series will be illustrated with the synthesis of 3-(4-pyridyl)-1-propanethiol 1-oxide and related compounds (Table IIa, IIb).

3-(4-Pyridylpropyl)isothiuronium Bromide Hydrobromide 1-Oxide.

A solution containing 3.9 g. (0.025 mole) of 4-(3-hydroxy-1-propyl)pyridine 1-oxide and 1.9 g. (0.025 mole) of thiourea in 11.0 g. (0.065 mole) of 48% hydrobromic acid was refluxed for 15 hours. The solvent was removed *in vacuo* and ethyl acetate was added to aid crystallization. The crystalline material was washed with a small amount of acetone. There was obtained 8.4 g. (88%) of crude product, m.p. 125-130°. After several recrystallizations from ethanol-ethyl acetate, 7.3 g. (77%) of colorless prisms, m.p. 129-132° was obtained.

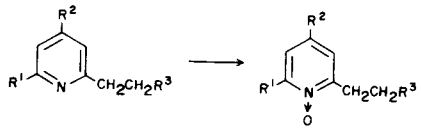
Anal. Calcd. for $C_9H_{15}Br_2N_3OS$: C, 29.0; H, 4.1. Found: C, 29.0; H, 4.4.

3-(4-Pyridyl)-1-propanethiol 1-Oxide.

A mixture containing 20.0 g. (0.054 mole) of 3-(4-pyridylpropyl)isothiuronium bromide hydrobromide 1-oxide and 6.43 g. (0.16 mole) of sodium hydroxide in 25 ml. of water was heated under a nitrogen atmosphere on the steam bath for one hour. The cooled reaction mixture was saturated with ammonium chloride and extracted three times with chloroform. The chloroform solution was dried (sodium sulfate) and the chloroform removed *in vacuo*. The product amounted to 8.4 g. (93%) of a pale yellow oil; pmr (DMSO-d_6): δ 2.04 (quintet, J = 6.0 Hz), 2.80 (t, J = 6.0 Hz), 3.00 (t, J = 6.0 Hz), 7.94 (d, J = 7.0 Hz), 8.94 (d, J = 7.0 Hz), 9.46 (broad s).

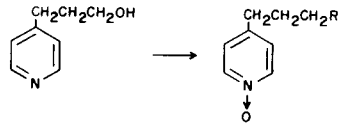
The hydrochloride was prepared by dissolving 8.4 g. of the

Table IIa



Compound No.	R	R^1	R^2	R^3	% Yield	M.p. °C	Recrystallization Solvent	Formula	Analyses C Calcd.	C Found	H Calcd.	H Found
8(a)		H	H	OH	98	Thick yellow oil		C_7H_9NO				
9		H	H	Cl	70	83-86	Chloroform-acetone	$C_7H_8ClNO \cdot H_2O$	47.9	48.0	5.7	5.8
10(b)		CH_3	CH_3	OH	24	105-106	Ethyl acetate	$C_9H_{13}NO$	64.7	65.0	7.8	7.7
11		CH_3	H	OH	57	82-84	Ethyl acetate	$C_8H_{11}NO_2$	62.7	62.8	7.2	7.0

Table IIb



12	OH			93	100	Ethyl acetate	$C_8H_{11}NO_2$	62.7	62.4	7.2	6.9
13	Cl			95	Thick oil		$C_8H_{10}ClNO$				
14	Cl				115-118	Methanol-ethyl acetate	$C_8H_{10}ClNO \cdot HCl$	46.2	46.4	5.3	5.3
15	Cl				119	Methanol	$C_8H_{10}ClNO \cdot C_6H_3N_3O_7$	42.0	41.9	3.2	3.1

(a) Pmr (DMSO-d_6): δ 3.08 (t, J = 6.0 Hz), 3.88 (t, J = 6.0 Hz), 4.94 (broad s), 7.24-7.60 (m, 3H), 8.32 (t, J = 4.0 Hz). (b) Pmr (DMSO-d_6): δ 2.23 (s), 2.36 (s), 2.98 (t, J = 6.0 Hz), 3.78 (quad., J = 6.0 Hz), 5.01 (t, J = 6.0 Hz), 7.14 (s).

above oil in 40 ml. of dry chloroform-ether and saturating the solution with dry hydrogen chloride. The precipitate was collected and crystallized from ethanol-ethyl acetate, colorless prisms, 9.2 g. (84%), m.p. 126-128°.

Anal. Calcd. for $C_8H_{11}NOS \cdot HCl$: C, 46.7; H, 5.9; N, 6.8. Found: C, 46.9; H, 5.9; N, 6.8.

The picrate, yellow needles from methanol had m.p. 113-114°.

Anal. Calcd. for $C_8H_{10}NOS \cdot C_6H_3N_3O_7$: C, 42.2; H, 3.5. Found: C, 42.3; H, 3.5.

4-(2,4-Dinitrophenylthiopropyl)pyridine 1-Oxide.

In the manner described for 2-(2,4-dinitrophenylthioethyl)-5-ethylpyridine, 1.7 g. of the unpurified 3-(4-pyridyl)-1-propanethiol 1-oxide gave 1.3 g. of yellow needles, m.p. 155-157° from ethanol-ethyl acetate.

Anal. Calcd. for $C_{14}H_{13}N_3O_5S$: C, 50.1; H, 3.9. Found: C, 50.0; H, 3.8.

3-(3-Pyridylpropyl)isothiuronium Bromide Hydrobromide 1-Oxide.

From 15.3 g. (0.1 mole) of 3-(3-hydroxypropyl)pyridine 1-oxide, 7.6 g. (0.1 mole) of thiourea and 44.0 g. (0.26 mole) of 48% hydrobromic acid as described above, there was obtained 30.0 g. (80%) of colorless prisms from absolute ethanol, m.p. 156-158°; pmr (DMSO-d_6): δ 2.12 (quintet, J = 7.0 Hz), 3.06 (t, J = 7.0 Hz), 3.40 (t, J = 7.0 Hz), 7.94-8.40 (m, 2H), 8.96 (d, J = 8.0 Hz), 9.04 (s), 9.22 (s, broad).

Anal. Calcd. for $C_9H_{15}Br_2N_3OS$: C, 29.0; H, 4.1. Found: C, 29.2; H, 4.1.

3-(3-Pyridyl)-1-propanethiol.

From 20 g. (0.054 mole) of 3-(3-pyridylpropyl)isothiuronium bromide hydrobromide 1-oxide treated as described above, 8.9 g. (98%) of crude product was obtained as a pale yellow oil which solidified in the refrigerator under a nitrogen atmosphere. Crystallization from methanol-ether gave 8.0 g. (88%) of very hygroscopic colorless needles, m.p. 37-39°.

Anal. Calcd. for $C_8H_{11}NOS$: C, 56.8; H, 6.6. Found: C, 56.5; H, 6.2.

The picrate upon crystallization from methanol had m.p. 84-87°.

Anal. Calcd. for $C_8H_{11}NOS \cdot C_6H_3N_3O_7$: C, 42.2; H, 3.5. Found: C, 42.0; H, 3.3.

3-(2,4-Dinitrophenylthiopropyl)pyridine 1-Oxide.

From 0.8 g. of 3-(3-pyridyl)-1-propanethiol there was obtained 1.2 g. of product, m.p. 162-163° from ethanol; pmr (DMSO-d_6): δ 2.06 (quintet, J = 7.0 Hz), 2.84 (t, J = 7.0 Hz), 3.26 (t, J = 7.0 Hz), 7.30 (s), 7.36 (d, J = 4.0 Hz), 7.80-8.60 (m, 4H), 8.84 (d, J = 3.0 Hz).

Anal. Calcd. for $C_{14}H_{13}N_3O_5S$: C, 50.1; H, 3.9. Found: C, 49.8; H, 3.7.

3-(2-Pyridylpropyl)isothiuronium Bromide Hydrobromide 1-Oxide.

From 8.0 g. (0.052 mole) of 2-(3-hydroxypropyl)pyridine 1-oxide, there was obtained 8.2 g. (43%) of pure product from ethanol, m.p. 146-148°.

Anal. Calcd. for $C_9H_{15}Br_2N_3OS$: C, 29.0; H, 4.1. Found: C, 28.6; H, 4.4.

3-(2-Pyridyl)-1-propanethiol 1-Oxide.

From 20.0 g. (0.054 mole) of 3-(2-pyridylpropyl)isothiuronium bromide hydrobromide 1-oxide there was obtained 8.5 g. (94%) of crude product as a pale yellow oil which would not solidify upon refrigeration. The picrate and styphnate (yellow oils) would not solidify. Furthermore, attempts to prepare a solid *d*-tartrate, citrate, ascorbate, succinate, oxalate, malonate, maleate, azelate, pimelate, phthalate or cinnamate were also unsuccessful. Likewise the perchlorate, hydrobromide or hydrochloride did not crystallize. However, the crude product did react with 2,4-dinitrochlorobenzene.

2-(2,4-Dinitrophenylthiopropyl)pyridine 1-Oxide.

From 0.8 g. of the oily 3-(2-pyridyl)-1-propanethiol 1-oxide as described above, 1.5 g. of product was obtained after crystallization from ethanol, m.p. 155-156°.

Anal. Calcd. for $C_{14}H_{13}N_3O_5S$: C, 50.1; H, 3.9. Found: C, 49.9; H, 3.7.

2-(4-Pyridylethyl)isothiuronium Bromide Hydrobromide 1-Oxide.

From 6.4 g. (0.046 mole) of 4-(2-hydroxyethyl)pyridine 1-oxide, 9.0 g. (55%) of product as colorless prisms from ethanol, m.p. 171° dec., was obtained; pmr (DMSO-d_6): δ 3.34 (t, J = 6.0 Hz), 3.80 (t, J = 6.0 Hz), 8.14 (d, J = 7.0 Hz), 9.10 (d, J = 7.0 Hz), 9.28 (broad s).

Anal. Calcd. for $C_8H_{13}Br_2N_3OS$: C, 26.8; H, 3.6. Found: C, 26.6; H, 3.4.

2-(4-Pyridyl)-1-ethanethiol 1-Oxide.

From 9.4 g. (0.026 mole) of 2-(4-pyridylethyl)isothiuronium bromide hydrobromide 1-oxide, there was obtained 3.8 g. (94%) of product as a pale yellow oil which was converted into the hydrochloride in dry ether-chloroform, yield 4.0 g. (80%) of colorless needles after crystallization from dry ether-chloroform, m.p. 90-92°.

Anal. Calcd. for $C_7H_9NOS \cdot HCl$: C, 43.9; H, 5.3. Found: C, 43.8; H, 5.4.

An attempt to prepare 2-(4-pyridyl)-1-ethanethiol 1-oxide from 4-(2-hydroxyethyl)pyridine 1-oxide and thionyl chloride in chloroform gave 4-(2-chloroethyl)pyridine 1-oxide as an oil after chromatography on alumina. Treatment of the product with potassium hydrogen sulfide in ethanol did not give 2-(4-pyridyl)-1-ethanethiol, but rather the sulfide was obtained as an oil which solidified after three days at room temperature. Recrystallization from methanol-acetone gave colorless prisms, m.p. 163-165°.

Anal. Calcd. for $C_{14}H_{16}N_2O_2S$: C, 60.9; H, 5.8. Found: C, 60.8; H, 5.7.

2-(2-Pyridylethyl)isothiuronium Bromide Hydrobromide 1-Oxide.

From 5.2 g. (0.037 mole) of 2-(2-hydroxyethyl)pyridine 1-oxide, there was obtained 7.5 g. (56%) of colorless prisms from ethanol-ethyl acetate, m.p. 167-168° dec.; pmr (DMSO-d_6): δ 3.48 (t, J = 5.5 Hz), 3.56 (t, J = 5.0 Hz), 7.48-8.00 (m, 3H), 8.76 (d, J = 6.0 Hz), 9.32 (broad s).

Anal. Calcd. for $C_8H_{13}Br_2N_3OS$: C, 26.8; H, 3.6. Found: C, 26.6; H, 3.4.

2-(2-Pyridyl)-1-ethanethiol 1-Oxide and the Corresponding Sulfide.

From 14.4 g. (0.04 mole) of 2-(2-pyridylethyl)isothiuronium bromide hydrobromide 1-oxide as described earlier, there was obtained 50 ml. of the crude chloroform extract which was dried (sodium sulfate). To this was added 20 ml. of dry ether and dry hydrogen chloride was bubbled through the solution. A precipitate was collected after standing overnight in the refrigerator. Recrystallization from ethanol gave 3.0 g. (23%) of the sulfide hydrochloride, m.p. 166-168° as colorless scales.

Anal. Calcd. for $C_{14}H_{18}Cl_2N_2O_2S$: C, 48.1; H, 5.2. Found: C, 48.3; H, 4.9.

The ether-chloroform filtrate above was concentrated *in vacuo*. A viscous oil (2.0 g., 26%) was obtained which would not solidify but which decolorized iodine solution indicating the presence of a free mercapto group. A picrate or a hydrochloride would not crystallize. The crude mercaptan (0.5 g.) gave 0.3 g. of 2-(2,4-dinitrophenylthioethyl)pyridine 1-oxide as yellow prisms from

1-butanol, m.p. 189° dec.; pmr (DMSO-d_6): δ 3.26 (t, J = 7.0 Hz), 3.64 (t, J = 7.0 Hz), 7.24-7.64 (m, 3H), 8.10-8.50 (m, 3H), 8.84 (d, J = 2.0 Hz).

Anal. Calcd. for $C_{13}H_{11}N_3O_5S$: C, 48.6; H, 3.5; N, 13.1. Found: C, 48.7; H, 3.4; N, 13.0.

2-[2-(6-Methylpyridyl)ethyl]isothiuronium Bromide Hydrobromide 1-Oxide.

From 7.7 g. (0.05 mole) of 2-(2-hydroxyethyl)-6-methylpyridine 1-oxide, there was obtained 8.0 g. (43%) of the product, m.p. 90-91° from ethanol-ethyl acetate.

Anal. Calcd. for $C_9H_{15}Br_2N_3OS$: C, 29.0; H, 4.1. Found: C, 29.0; H, 4.0.

Attempted Preparation of 2-(6-Methyl-2-pyridyl)-1-ethanethiol 1-Oxide. Preparation of the Corresponding Sulfide.

From 6.3 g. (0.017 mole) of 2-[2-(6-methylpyridyl)ethyl]-isothiuronium bromide hydrobromide 1-oxide treated as described earlier, the chloroform solution was obtained and evaporated *in vacuo*. The pale yellow oil was dissolved in dry ether-chloroform (1:1) and dry hydrogen chloride was bubbled into the solution. The precipitate was crystallized from ethanol, yield 1.2 g. (36%) of white prisms, m.p. 198-200° dec.

Anal. Calcd. for $C_{16}H_{22}Cl_2N_2O_2S$: C, 50.9; H, 5.8. Found: C, 50.6; H, 5.4.

Preparation of 2-(4,6-Dimethyl-2-pyridyl)-1-ethanethiol 1-Oxide and the Corresponding Sulfide.

4,6-Dimethyl-2-(2-hydroxyethyl)pyridine 1-oxide (4.5 g., 0.027 mole) was converted into 2-(4,6-dimethyl-2-pyridylethyl)isothiuronium bromide hydrobromide 1-oxide and without purification, 3.8 g. was treated as before and the sulfide dihydrochloride (0.8 g.) was obtained after crystallization from methanol-ether, m.p. 178-181° dec.

Anal. Calcd. for $C_{18}H_{26}Cl_2N_2O_2S$: C, 53.3; H, 6.5. Found: C, 53.0; H, 6.2.

Evaporation of the ether-chloroform filtrate as reported in an earlier instance gave 0.4 g. of an oil which when allowed to react with 2,4-dinitrochlorobenzene gave 4,6-dimethyl-2-(2,4-dinitrophenylthioethyl)pyridine 1-oxide, the formation of which established the presence of the crude mercaptan.

Anal. Calcd. for $C_{15}H_{15}N_3O_5S$: C, 51.6; H, 4.3. Found: C, 51.6; H, 4.2.

Attempted Preparation of 2-(5-Ethyl-2-pyridyl)-1-ethanethiol 1-Oxide and the Preparation of the Corresponding Sulfide.

5-Ethyl-2-(2-hydroxyethyl)pyridine 1-oxide (13.0 g., 0.078 mole) was converted into 2-(5-ethyl-2-pyridylethyl)isothiuronium bromide hydrobromide 1-oxide which separated as an oil (9.3 g.). This was directly decomposed with sodium hydroxide solution, and after heating, saturated with ammonium chloride, extracted with chloroform, dried and the volume reduced to about one half. Dry hydrogen chloride was bubbled into the dry chloroform solution and 3.0 g. (19%) of the sulfide dihydrochloride was obtained from 1-butanol.

Anal. Calcd. for $C_{18}H_{26}Cl_2N_2O_2S$: C, 53.3; H, 6.5. Found: C, 53.1; H, 6.2.

The Preparation of Bunte Salts. 5-Ethyl-2-pyridylethyl Bunte Salt.

A solution containing 20.0 g. (0.118 mole) of 2-(2-chloroethyl)pyridine in 50 ml. of ethanol and another solution composed of 29.4 g. (0.118 mole) of sodium thiosulfate pentahydrate in 50 ml. of water were mixed and refluxed for fifteen hours. The solvents were removed *in vacuo* below 50°. To the residue was added 50 ml. of absolute ethanol, the solid which precipitated was removed and the filtrate was concentrated and the process repeated twice more. To the final ethanol solution (50 ml.) was added 50 ml. of ethyl acetate and a solid separated upon refrigeration. It was collected, washed with ether, air dried (vacuum) at room temperature to yield 10.5 g. (33%) of a colorless, very hygroscopic solid, sensitive to heat.

Anal. Calcd. for $C_9H_{12}NO_3S_2Na$: C, 40.1; H, 4.5; N, 5.2. Found: C, 40.2; H, 4.6; N, 5.2.

4,6-Dimethyl-2-pyridylethyl Bunte Salt.

From 14.7 g. (0.0865 mole) of 2-(2-chloroethyl)-4,6-dimethylpyridine, there was obtained 9.3 g. (34%) of a colorless, very hygroscopic solid from ethanol-ether.

Anal. Calcd. for $C_9H_{12}NO_3S_2Na \cdot 0.5H_2O$: C, 38.8; H, 4.7; N, 5.0. Found: C, 39.1; H, 4.3; N, 5.0.

6-Methyl-2-pyridylethyl Bunte Salt.

From 14.7 g. (0.0945 mole) of 2-(2-chloroethyl)-6-methylpyridine, there was obtained 16 g. (62%) of hygroscopic colorless needles, m.p. 75-80° from ethanol-ether.

Anal. Calcd. for $C_8H_{10}NO_3S_2Na \cdot H_2O$: C, 35.2; H, 4.4; N, 5.1. Found: C, 35.3; H, 4.0; N, 5.5.

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(16) These data were supplied by Dr. T. R. Sweeney, Walter Reed Army Institute of Research, Walter Reed Army Medical Center, Washington, D. C. The screening protocol is classed as follows: *good*, when 45% or more of the treated animals lived and none of the control animals survived; *fair*, when 26-44% of the treated animals lived and none of the control animals survived; *some*, when 5-25% of the treated animals lived and none of the control animals survived; *none*, when 0-4% of the treated animals lived and none of the control animals survived at the specific dosage level of the compound. The radiation given treated and control animals is the LD/100, therefore protection is cited as protection *vs* LD/100.

(17) The analyses were performed by Miss Yoko Togushige. The nmr spectra were determined in the solvent indicated on a Varian D-60 spectrometer with TMS as the internal reference. Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected.