mixture was stirred for another hr with the bath at 250°, cooled, and extracted with 1 l. of acetone in four portions. The acetone solution was evaporated to give an oil which was refluxed with 300 ml of 2 *N* KOH in aqueous ethanol for 8 hr. The cooled hydrolysate was concentrated to remove alcohol, diluted with water to 1 l. and filtered to remove a little insoluble material. The filtrate was washed twice with benzene and then made acidic with 6 *N* H_2SO_4 to give 45 g of crude solid, which was extracted at room temperature with 500 ml of benzene in three portions. The residue consisted of 17.8 g of diphenic acid. The filtrate was concentrated to a small volume to give 13.7 g of crystalline solid, mp 154–156°. From the mother liquor a second crop of 3 g (mp 150–153°) was obtained; total yield 16.7 g (44%). Recrystallization from ethanol–water gave 13.7 g (36%) of the acid as colorless crystals, mp 155.5–156°.

Anal. Calcd for $C_{15}H_{10}O_2S$: C, 70.84; H, 3.96. Found: C, 71.08; H, 4.03.

***o*-(2-Thienyl)benzoic Acid.**—Copper bronze (60 g) was added in small portions during 20 min to a stirred mixture of 26 g (0.124 mole) of *o*-iodothiophene and 60 g (0.23 mole) of methyl *o*-iodobenzoate heated in a bath at 180°. The resulting sludge was stirred under reflux for a further 4 hr with the bath at 210–220°. The reaction mixture was processed in the same manner as described for the preparation of *o*-(2-thianaphthenyl)benzoic acid. The crude product weighed 5.5 g (22%), mp 84–91°. Recrystallization from aqueous acetic acid gave 3.65 g (14%) of the pure acid as colorless crystals, mp 93–94°.

Anal. Calcd for $C_{11}H_8O_2S$: C, 64.69; H, 3.95. Found: C, 64.83; H, 4.02.

Preparation of Penicillins.—The methods used for the preparation of penicillins are those reported in the first paper of this series.[2] In most cases the acid chlorides of the side-chain acids were used to react with 6-aminopenicillanic acid in aqueous acetone in the presence of $NaHCO_3$ and the penicillins were isolated as their sodium or potassium salts. In two cases, penicillins **18** and **20** of Table I, an anhydrous system consisting of acid chloride–triethylamine–chloroform was used. The resulting penicillins were isolated in the usual manner.

Acknowledgment.—We wish to thank Mr. J. J. Taggart for technical assistance; Miss M. Davis, Miss J. P. Froelich, Mrs. L. R. Gordon, Mr. W. N. King, Miss L. Phillips, Mrs. R. R. Tumilowicz, and Mr. D. S. Ziv for their microbiological work; and Mrs. D. A. Rolston and her staff for elemental analyses.

Activity of a Series of Piperdines against *Haemonchus contortus* Larvae

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An *in vitro* test procedure using larvae of *Haemonchus contortus*, a gastrointestinal nematode of sheep, has been used to determine the antilarval activity of a series of 1,4-substituted piperidines and related compounds. Structure–activity relationships are discussed. The most effective compound found in this series of piperidines, many of which are new to the literature, was 1-phenethyl-4-phenylpiperidine hydrochloride which produced a 90% reduction in developing larvae at a concentration of 1:8000.

Larvae of horse strongyles have been used to examine the antilarval activity of compounds for many years.[2] Many series of organic and inorganic compounds have been tested by this method.[3–5] The methods and early literature have been well reviewed.[6]

The test was orginally designed to find a compound which would kill larvae on pasture, but has also proved useful in discovering compounds capable of killing the parasitic stages within the host animal. The organic phosphate, O,O-dimethyl-1-hydroxy-2,2,2-trichloroethyl phosphonate[7] which was found to be efficient against larvae of horse strongyles[8] has subsequently been found to be a useful anthelmintic treatment for adult *Haemonchus* and other nematode species of sheep[9] and cattle[10] when given orally or subcutaneously.[11]

Using a similar approach, the aim of our investigation was to discover a compound having sufficient activity against larvae of sheep helminths, so that when incorporated in a heavy pill, similar to the cobalt bullet,[12] and lodged permanently in the reticulorumen, the small quantity of compound continuously released would maintain a concentration in the rumen liquor sufficient to kill the majority of infective larvae as they were ingested with forage. About 1600 random organic compounds were tested. One of the first test compounds to show moderate activity was 3-phenethyl-3-azaspiro[5.5]undecane hydrochloride, one of a group of 1,4-substituted piperidines that had been synthesized for general pharmacological studies,[13] and others were synthesized and tested in pursuit of activity at a useful level. While useful activity was not attained in this series of compounds, interesting structure–activity relationships were noted and these are reported.

Testing Procedure.—Feces containing eggs of *H. contortus* were collected in fecal bags from lambs with pure infestations. The lambs were held indoors in concrete pens to prevent infestation with other helminths.

The pellets of feces were broken and mixed thoroughly. If necessary, sufficient helminthologically sterile feces were added to ensure that the moisture content was not too high. Five-gram samples were weighed into small tubes, 5 × 2 cm, containing a small wad of nonabsorbable cotton wool and the end was covered with muslin held on by a rubber band. The compound to be tested in the form of its hydrochloride salt was introduced in aqueous solution or as a fine sus-

(1) To whom all requests for reprints should be addressed.
(2) I. W. Parnell, *Can. J. Res.*, **D14**, 71 (1936).
(3) N. D. Levine, *Am. J. Vet. Res.*, **10**, 233 (1949).
(4) N. D. Levine, *ibid.*, **12**, 110 (1951).
(5) N. D. Levine, *J. Parasitol.*, **37**, 195 (1951).
(6) N. D. Levine, *Trans. Illinois State Acad. Sci.*, **43**, 233 (1950).
(7) Dipterex®, Trichlorophon.
(8) N. D. Levine, V. Ivens, M. D. Kleckner, and J. K. Souder, *Am. J. Vet. Res.*, **17**, 117 (1956).
(9) W. H. Southcott, *Australian Vet. J.*, **37**, 55 (1961).
(10) R. F. Reik and R. K. Keith, *ibid.*, **34**, 93 (1958).
(11) R. K. Keith, *ibid.*, **40**, 402 (1964).
(12) D. W. Dewey, H. J. Lee, and H. R. Marston, *Nature*, **131**, 1367 1958).
(13) T. C. Somers and G. J. Handley, *J. Med. Chem.*, **7**, 784 (1964).

pension in 5 ml of water through a long 19-gauge hypodermic needle, the end of which had been blocked and in the sides of which small holes had been drilled at regular intervals. This allowed an even spread of the compound through the feces.

The tube with treated feces was placed open end up, in a 50-ml wide-mouthed glass jar containing 10 ml of water; the plastic cap, with the insert removed, was screwed lightly on and the whole was incubated at 29° for 7 days. *Haemonchus* eggs develop to infective third stage larvae in 5–6 days under these conditions and migrate from the tube into the water. To ensure that as many larvae as possible were collected, the tubes containing feces were filled with water and inverted in the bottles for a further 24 hr. As the larvae cannot swim in a body of water they quickly settle to the bottom. The tubes were then drained and the number of larvae present in the bottles was estimated by counting the numbers present in one-sixth of the total volume.

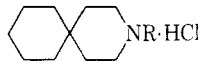
In each test, control feces were cultured as above using water or the suspending agent used in that test. In the initial screening, compounds were tested at concentrations of 1 part of compound to 500 parts of feces. If high activity was shown then further tests were done to ascertain the concentration at which a 90% reduction in numbers of larvae developing was obtained.

Results and Discussion

The larvicidal activity of 3-azaspiro[5.5]undecane hydrochlorides having various alkyl and aralkyl substitutes at the 3 position are shown in Table I. In this series optimal activity is seen to be associated with the phenethyl grouping.

TABLE I

ACTIVITY OF SUBSTITUTED 3-AZASPIRO[5.5]UNDECANE HYDROCHLORIDES AGAINST LARVAE OF *Haemonchus contortus*



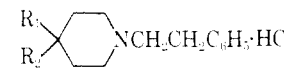
R	Activity[a]
H	≪500
CH_3	<1000
C_2H_5	1000
n-C_3H_7	1000
$CH(CH_3)_2$	1500
$CH_2CH{=}CH_2$	1000
$CH_2CH(CH_3)_2$	1000
$CH_2CH_2CH(CH_3)_2$	<1000
$(CH_2)_5CH_3$	1000
C_6H_5	<500
$CH_2C_6H_5$	500
$CH(CH_3)C_6H_5$	500
$CH_2CH_2C_6H_5$	2000
$CH(C_2H_5)C_6H_5$	500
$CH(CH_3)CH_2C_6H_5$	500
$CH_2CH_2COC_6H_5$	500
Phenothiazine[b]	1000

[a] The reciprocal of this figure is the concentration (w/w) of the test compound in feces that produced a 90% reduction in developing larvae. [b] Phenothiazine had a surface area of approximately 16,000 cm^2/g and a purity of 88–90%.

Retaining $CH_2CH_2C_6H_5$ on the nitrogen, the 4 substituents in this series of piperidines were varied as shown in Table II. Activity at 1:8000 was found with 1-phenethyl-4-phenylpiperidine hydrochloride (I). This peak activity was not affected by the introduction of a *p*-chloro substituent, but was almost abolished by a similar introduction of an amino grouping. The high degree of structural specificity existing here is further illustrated by the very low activity of 1-phenethyl-4-methyl-4-phenylpiperidine hydrochloride compared with the corresponding 4-phenyl compound.

TABLE II

ACTIVITY OF SUBSTITUTED 1-PHENETHYLPIPERIDINE HYDROCHLORIDES AGAINST LARVAE OF *Haemonchus contortus*



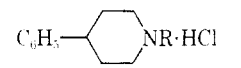
R_1	R_2	Activity[a]
H	H	1000
H	CH_3	1500
H	$CH(CH_3)_2$	4000
H	C_6H_5	8000
H	p-ClC_6H_4	8000
H	p-$NH_2C_6H_4$	500
H	$CH_2C_6H_5$	2000
CH_3	C_2H_5	750
CH_3	n-C_4H_9	2000
CH_3	n-C_5H_{11}	2000
CH_3	n-C_6H_{13}	1000
	$-(CH_2)_4-$	1000
	$-(CH_2)_5-$	2000
CH_3	C_6H_5	500

[a] See footnote *a*, Table I.

High larvicidal activity was sought in a third series in which the 4-phenyl substituent was retained and the 1 substituent was varied. However, Table III further shows that the 1-phenethyl and the 4-phenyl substituents together give optimal *in vitro* larvicidal activity in this class of 1,4-substituted piperidines. The smallest interference with the 1-phenethyl substituent is seen to reduce the activity markedly. The allyl substituent, which conferred activity to 1:4000, was the best of the others.

TABLE III

ACTIVITY OF SUBSTITUTED 4-PHENYLPIPERIDINE HYDROCHLORIDES AGAINST LARVAE OF *Haemonchus contortus*



R	Activity[a]	R	Activity[a]
H	1000	$CH_2C_6H_5$	1000
CH_3	2000	$CH_2CH_2C_6H_5$	8000
$CH_2CH{=}CH_2$	4000	$CH(CH_3)CH_2C_6H_5$	2000
$CH(CH_3)_2$	2000	$CH_2CH_2CH_2C_6H_5$	2000
$CH_2CH_2CH(CH_3)_2$	2000	$CH_2CH_2OC_6H_5$	2000
C_6H_5	1000	CH_2CH_2-3,4-$(OCH_3)_2C_6H_3$	1000

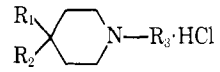
[a] See footnote *a*, Table I.

Other compounds having different heterocyclic ring systems, but being otherwise related to the best of the piperidine compounds (I), were synthesized for screening.

1-Phenethyl-3-phenylpyrrolidine (II), 1-phenethyl-4-phenylpiperazine (III), and 1,4-diphenethylpiperazine (IV) produced a 90% reduction in developing larvae at dilutions of 1:2000. 4-Phenethyl-1,4-thiazane (V) was

TABLE IV

SUBSTITUTED PIPERIDINE HYDROCHLORIDES

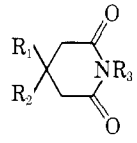


R_1	R_2	R_3	Bp (mm) or mp, °C of free base	Mp, °C	Formula	% calcd C	% calcd H	% calcd N	% found C	% found H	% found N
H	C_6H_5	$CH_2CH{=}CH_2$	115 (2)	183–185	$C_{14}H_{20}ClN$	70.7	8.5	5.9	70.3	8.1	5.9
H	C_6H_5	$CH_2CH_2CH(CH_3)_2$	138–142 (3.2)	264–266	$C_{16}H_{26}ClN$	71.8	9.8	5.2	72.0	9.8	5.1
H	C_6H_5	C_6H_5	89–90	209–219	$C_{17}H_{20}ClN$	74.6	7.4	5.1	74.5	7.3	4.9
H	C_6H_5	$(CH_2)_3C_6H_5$	201 (3)	214–216[a]	$C_{20}H_{26}ClN$	76.0	8.3	4.4	76.4	8.3	4.3
H	C_6H_5	$CH(CH_3)CH_2C_6H_5$	200–202 (3)	263–266	$C_{20}H_{26}ClN$	76.0	8.3	4.4	76.1	8.3	4.2
H	C_6H_5	$CH_2CH_2OC_6H_5$	200 (2)	165–170[a]	$C_{17}H_{24}ClNO$	71.8	7.6	4.4	71.6	7.7	4.4
H	p-ClC_6H_4	$CH_2CH_2C_6H_5$	85–87	258	$C_{19}H_{23}Cl_2N$	67.9	6.9	4.2	67.5	6.7	4.1
H	p-$NH_2C_6H_4$	$CH_2CH_2C_6H_5$	77–78.5	290[b]	$C_{19}H_{26}Cl_2N_2$	64.6	7.4	7.9	65.1	7.6	7.6
H	$C_6H_5CH_2$	$CH_2CH_2C_6H_5$	220–224 (5)	235–238	$C_{20}H_{26}ClN$	76.0	8.4	4.4	75.8	8.4	4.1
CH_3	C_6H_5	$CH_2CH_2C_6H_5$	...	260	$C_{20}H_{26}ClN$	76.0	8.4	4.4	75.8	8.3	4.3

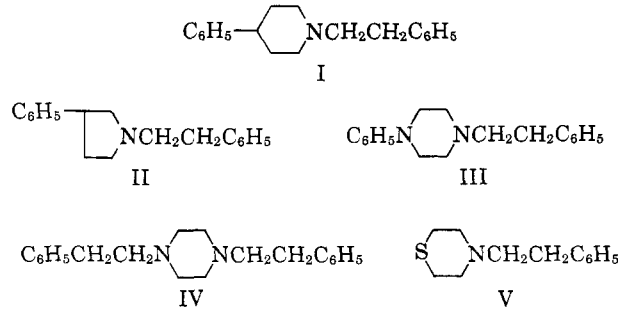
[a] Prepared by alkylation of 4-phenylpiperidene in toluene with anhydrous Na_2CO_3. [b] Dihydrochloride salt; the intermediate imide, N-phenethyl-β-(*p*-aminophenyl)glutarimide, was obtained by hydrogenation of N-phenethyl-β-(*p*-nitrophenyl)glutarimide in alcohol using PtO_2 catalyst for 1 hr at 70° and 3.16 kg/cm²; colorless needles, mp 181–183° (91% yield).

TABLE V

β-SUBSTITUTED GLUTARIMIDES



R_1	R_2	R_3	Mp or bp (mm), °C	Formula	% calcd C	% calcd H	% calcd N	% found C	% found H	% found N
H	i-C_3H_7	$CH_2CH_2C_6H_5$	80–81	$C_{16}H_{21}NO_2$	74.1	8.2	5.4	74.4	8.2	5.6
H	C_6H_5	$CH_2CH{=}CH_2$	44–48	$C_{14}H_{15}NO_2$	73.3	6.6	6.1	73.7	6.5	6.3
H	C_6H_5	i-C_3H_7	76–77	$C_{14}H_{17}NO_2$	72.7	7.4	6.1	72.8	7.4	6.2
H	C_6H_5	i-C_5H_{11}	132–133	$C_{16}H_{21}NO_2$	74.1	8.2	5.4	74.4	8.2	5.6
H	C_6H_5	$CH_2CH_2C_6H_5$	141	$C_{19}H_{19}NO_2$	77.8	6.5	4.8	77.3	6.9	4.9
H	C_6H_5	$CH(CH_3)CH_2C_6H_5$	71–73	$C_{20}H_{21}NO_2$	78.2	6.9	4.6	78.2	6.8	4.6
H	p-$NO_2C_6H_4$	$CH_2CH_2C_6H_5$	192	$C_{19}H_{18}N_2O_4$	67.4	5.4	8.2	67.8	5.4	7.9
H	p-ClC_6H_4	$CH_2CH_2C_6H_5$	156–157	$C_{19}H_{18}ClNO_2$	69.6	5.5	4.3	69.3	5.6	4.1
CH_3	C_6H_5	$CH_2CH_2C_6H_5$	121	$C_{20}H_{21}NO_2$	78.1	6.9	4.6	78.3	7.0	4.5
	$-(CH_2)_5-$	$CH(C_2H_5)C_6H_5$	214 (3.5)	$C_{19}H_{25}NO_2$	76.4	8.4	4.7	75.9	8.3	5.1



similarly active at 1:1000. The incorporation of a sulfur atom, so common to anthelmintics, produced no benefit in this instance.

Experimental Section

Melting points were determined on a gas-heated Electrothermal apparatus and are uncorrected. Microanalyses were carried out by the University of Melbourne and CSIRO Microanalytical Service. Some of the piperidines listed in Tables II and III are new to the literature and chemical data for them are presented in Table IV. Synthetic procedures were generally as described, by Somers and Handley[13] for 4,4-dialkyl-1-substituted piperidines *i.e.*, the lithium aluminum hydride ($LiAlH_4$) reduction of the corresponding glutarimide.[14] Data for intermediate glutarimides new to the literature are given in Table V. Yields for both stages varied between 60–85%. The following example is typical of the method used to prepare these piperidines.

N-Allyl-3-phenylglutarimide.—β-Phenylglutaric anhydride (17.9 g, 0.1 mole) and allylamine (6.0 g, 0.105 mole) were mixed with cooling in an ice bath. The mixture was heated at 190–210° for 3 hr, when evolution of water vapor ceased, then vacuum distilled. The product crystallized on cooling and was further purified by recrystallization from water to give prisms (16.0 g, 70%), mp 44–48°.

Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.3; H, 6.6; N, 6.1. Found: C, 73.7; H, 6.5; N, 6.3.

From the pot residues N,N′-diallyl-3-phenylglutaramide was obtained by extraction and crystallization from water; needles (0.9 g), mp 152–155°.

Anal. Calcd for $C_{17}H_{22}N_2O_2$: C, 71.3; H, 7.7; N, 9.8. Found: C, 71.2; H, 7.6; N, 9.8.

1-Allyl-4-phenylpiperidine Hydrochloride.—An ethereal solution of the above glutarimide (10.3 g, 0.045 mole) was added with stirring over 15 min to a slurry of $LiAlH_4$ (4.5 g, 0.13 mole) in 250 ml of dry ether. The mixture was refluxed for 1 hr and the complex was then decomposed by the addition of moist ether and finally water. After filtration the inorganic residue was liberally washed with ether and the combined filtrate and washings were dried (Na_2SO_4). The solvent was removed and the residue was distilled to give 1-allyl-4-phenylpiperidine as a colorless liquid (7.2 g, 80%), bp 115° (2 mm). The hydrochloride salt was prepared by bubbling dry HCl through an ethereal solution of the base. After filtration and two recrystallizations from alcohol–ether the product was obtained as colorless plates, mp 183–185°.

Anal. Calcd for $C_{14}H_{20}ClN$: C, 70.7; H, 8.5; N, 5.9. Found: C, 70.3; H, 8.1; N, 5.9.

Miscellaneous syntheses include the following.

(14) G. J. Handley, E. R. Nelson, and T. C. Somers, *Australian J. Chem.*, **13**, 129 (1960).

1-Phenethyl-3-phenylpyrrolidine (II).—N-Phenethyl-2-phenylsuccinimide, mp 72–73° (23 g obtained by fusion of phenylsuccinic anhydride with phenethylamine), was reduced with $LiAlH_4$ (6 g) in dry ether to give 14 g, bp 172–174° (3 mm), $n^{18}D$ 1.5663. Since the hydrochloride salt appeared to be hygroscopic, the base was analyzed as the **picrate**, obtained as yellow needles from ethanol, mp 112.5–115°.

Anal. Calcd for $C_{24}H_{24}N_4O_7$: C, 60.00; H, 5.0; N, 11.7. Found: C, 59.2; H, 5.2; N, 11.7.

1-Phenyl-4-phenethylpiperazine (III).—A mixture of 1-phenylpiperazine (9 g, 0.055 mole), phenethyl bromide (10.3 g, 0.055 mole), and anhydrous Na_2CO_3 (8 g) were refluxed for 7 hr in 100 ml of absolute alcohol. After cooling, the mixture was filtered and the filtrate was evaporated to dryness. The resulting semicrystalline mass was extracted three times with 100-ml portions of warm petroleum ether (bp 55–75°) which, on evaporation, gave 9 g (61%) of III. The hydrochloride was prepared by treating an ethereal solution of the base with gaseous HCl. Recrystallization from alcohol–ether gave prisms, mp 219–221°, lit.[15] mp 220–222°.

1,4-Diphenethylpiperazine (IV).—Ethylene dibromide (21.6 g, 0.115 mole), phenethylamine (12.1 g, 0.111 mole), and Na_2CO_3 (20 g) were refluxed in 100 ml of water for 3 hr. After cooling, the reaction mixture was extracted with four 100-ml portions of ether, the extracts were dried (Na_2SO_4), and the solvent was removed to leave a liquid that slowly crystallized. Recrystallization from petroleum ether gave colorless needles, mp 76–78°, lit.[16] mp 79–80°. The hydrochloride prepared in the manner above, was recrystallized from ethanol; mp 27 .°.

(15) B. L. Hampton and C. B. Pollard, *J. Am. Chem. Soc.*, **59**, 2570 (1937).

4-Phenethyl-1,4-thiazane (V).—Thiodiglycollic acid anhydride (13 g, 0.1 mole) and phenethylamine (12.5 g, 0.103 mole) were cautiously mixed and then heated at 200° for 5 hr. Considerable decomposition occurred, but distillation of the fusion mixture and subsequent crystallization from benzene–petroleum ether gave 6 g (28%) of N-phenethylthiodiglycollic acid imide, bp 175–185° (3 mm), mp 56–59°. Reduction of this imide with $LiAlH_4$ (3 g) in ether gave 4.5 g of product, bp 145–152° (5 mm), $n^{18}D$ 1.5625. The hydrochloride was precipitated from an ethereal solution of the base by gaseous HCl and, after recrystallizations from water and ethanol, it was obtained as colorless flakes, mp 252–254° dec.

Anal. Calcd for $C_{12}H_{18}ClNS$: C, 59.1; H, 7.4; N, 5.7. Found: C, 59.6; H, 7.5; N, 5.4.

3-(3-Benzoyethyl)-3-azaspiro[5.5]undecane Hydrochloride.—3-Azaspiro[5.5]undecane hydrochloride (9.1 g, 0.048 mole), acetophenone (5.8 g, 0.048 mole), paraldehyde (3.2 g), and concentrated HCl (0.2 ml) were refluxed for 2 hr in 100 ml of absolute ethanol. The solution was then concentrated to 50 ml and the product precipitated with the addition of ether. Recrystallization from acetone–ethanol gave colorless plates (6.2 g, 35%), mp 190° dec.

Anal. Calcd for $C_{19}H_{28}ClNO$: C, 70.9; H, 8.8; N, 4.3. Found: C, 71.3; H, 8.7; N, 3.9.

Acknowledgment.—The authors wish to thank Dr. I. W. Parnell for his assistance in setting up the screening test. Thanks are also due to Messrs. A. E. Sibbing and M. I. Murray for their careful technical assistance.

(16) W. G. Barb, *J. Chem. Soc.*, 2577 (1955).

Potential Antiradiation Drugs. III.[1] 2-Amino-2-alkyl-1,3-propanedithiols and 3-Amino-4-mercapto-1-butanol[2]

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Syntheses and radioprotective properties are described for 2-amino-2-methyl-1,3-propanedithiol, 2-amino-2-ethyl-1,3-propanedithiol, and L-(+)-3-amino-4-mercapto-1-butanol. The dithiols did not provide significant protection in rodents, but the aminothiol alcohol gave good protection.

In continuing our study[1] of pure organic compounds that might protect against the lethal effects of ionizing radiation it was of interest to examine simple aminothiols having more than one thiol function. The significance of aminodithiols as potential antiradiation drugs was recognized some time ago by Russian workers[3] who prepared a wide variety of N-substituted aminopropanedithiols; an evaluation of these substances as drugs has not been published. A closely similar group of compounds was also prepared by Japanese workers[4] who claimed only bactericidal and insecticidal activity for the substances. Both groups synthesized the dithiols by the sulfhydrylation of appropriate halogeno precursors.

Aminothiol alcohols were also of interest in our program. The synthesis of a series of Bunte salts derived from isomeric aminomercaptopropanols has been described, which involved the respective aminothiol alcohols as nonisolated intermediates.[5] More complex substances having two secondary hydroxyl groups, two secondary amino groups, and two thiol groups have also been prepared[6] but nothing is known about their radioprotective properties. The three compounds whose synthesis and radioprotective properties we describe here contain *primary* amino, primary thiol, and primary alcohol functions.

Chemistry.—The two aminodithiols were prepared from available amino alcohols by the route indicated in Chart I, in which the procedure of Owen and co-

(1) Paper II: G. R. Handrick, E. R. Atkinson, F. E. Granchelli, and R. J. Bruni, *J. Med. Chem.*, **8**, 762 (1965).

(2) This work was performed under contract DA-49-193-MD-2071 with the U. S. Army Medical Research and Development Command, Office of the Surgeon General, during the period 1961–1962.

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