David A. Berges, George W. Chan, Theodore J. Polansky, John J. Taggart and George L. Dunn*

Research and Development Division, Smith Kline & French Laboratories, Philadelphia, Pennsylvania 19101

Received January 10, 1978

Homologous 4,5-dihydro-5-thioxo-1*H*-tetrazole-1-alkanoic and alkanesulfonic acids were prepared by reaction of sodium azide with methyl (carboxyalkyl)- and (sulfoalkyl)carbamodithioates, respectively. 4,5-Dihydro-5-thioxo-1*H*-tetrazole-1-alkanamides were derived from the corresponding alkanoic acids by aminolysis of their acid chlorides or imidazolides. Analogous alkanesulfonamides were synthesized by the reaction of methyl [[[(1,1-dimethylethyl)amino]sulfonyl]-alkyl]carbamodithioates with sodium azide followed by removal of the 1,1-dimethylethyl group with trifluoroacetic acid.

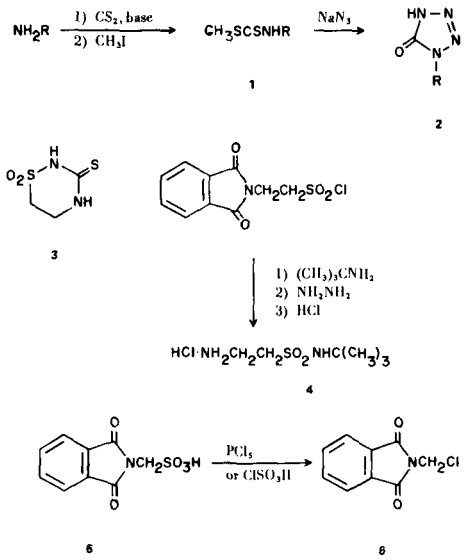
J. Heterocyclic Chem., 15, 981 (1978)

In the course of studying the structure-activity relationships of a group of cephalosporin antibiotics, homologous dihydrotetrazole-5-thiones substituted in the 1-position with carboxy-, carbamoyl-, sulfo- and sulfamoylalkyl groups were required. Reported methods for making 1-substituted dihydrotetrazole-5-thiones include the addition of sodium azide to isothiocyanates (1) or (alkyl)- or (aryl)carbamodithioic acids (as their esters (2) or salts (3)) and the base-catalyzed rearrangement of 5-arylamino-1,2,3,4-thiatriazoles (4). Synthesis and stability considerations led to the selection of the carbamodithioic acid ester route for preparing the dihydrotetrazole-5-thiones desired for the SAR study.

(Carboxyalkyl)carbamodithioates have been prepared (5) by the reaction of an amino acid with carbon disulfide in the presence of base followed by addition of an alkyl halide (6) and by aminolysis of alkyl *O*-*t*-alkyl carbonodithioates (7). In the present study the carbon disulfide method was used to prepare the (carboxyalkyl)carbamodithioates and was extended to the preparation of their sulfoalkyl and sulfamoylalkyl analogs. The carbamodithioates which are new and for which elemental analyses were obtained are shown in Table I.

Treatment of the carbamodithioates with sodium azide produced dihydrotetrazole-5-thiones (**2**, see Table II) except for the sulfonamide derivative **1j** which underwent internal cyclization to dihydrothiadiazine **3**. In this case blocking the sulfonamide amino function with a 1,1-dimethylethyl group (**1k**, prepared from **4**) allowed cyclization to tetrazole **2m** from which the blocking group was removed with trifluoroacetic acid/anisole (8) to produce **2n**. The tetrazolepropanesulfonamide derivative **2o** was made in a similar manner, but attempts to prepare the methanesulfonamide derivative failed when treatment of 1,3-dihydro-1,3-dioxo-2*H*-isoindol-2-ylmethanesulfonic acid (**5**) with phosphorus pentachloride or chlorosulfonic acid produced 2-(chloromethyl)-1*H*-isoindole-1,3-(2*H*)-dione (**6**) instead of the desired sulfonyl chloride.

The 4,5-dihydro-5-thioxo-1*H*-tetrazole-1-alkanamides



(see Table II) were prepared from the corresponding carboxylic acids by aminolysis of their acid chlorides or imidazolides. A similar attempt to prepare 4,5-dihydro-5-thioxo-1*H*-tetrazole-1-methanesulfonamide was unsuccessful because sulfonate **2i** could not be converted to its acid chloride.

EXPERIMENTAL

Infrared spectra were obtained in Nujol mull using a Perkin-Elmer Infracord. Nmr spectra were obtained on a Varian T-60 spectrometer with tetramethylsilane or, when deuterium oxide was solvent, sodium 2,2-dimethyl-2-silapentane-5-sulfonate as internal standard. Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected.

Preparation of Methyl Carbamodithioates.

Procedure A.

Methyl (2-sulfoethyl)carbamodithioate, Potassium Salt (**1g**).

2-Aminoethanesulfonic acid (50 g., 0.40 mole) was dissolved in a solution of potassium hydroxide (45 g., 0.80 mole) in 100 ml. of water, and carbon disulfide (24.4 ml., 0.40 mole) was added. The mixture was heated at gentle reflux for 2.5 hours

Table I

Methyl Carbamodithioates (a)

$CH_3SCSNHR$

Compd.	R	Formula	Proc. (b)	% Yield	M.p., °C	Analyses (%) Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
1a	$(CH_2)_2CO_2H$	$C_5H_9NO_2S_2$	A	80	87-88	33.50	5.06	7.81	33.77	5.34	8.02
1b	$(CH_2)_3CO_2H$	$C_6H_{11}NO_2S_2$	B	~100	81-83	37.28	5.74	7.25	37.18	5.73	7.19
1c	$(CH_2)_4CO_2H$	$C_7H_{13}NO_2S_2$	B	77	63-64	40.56	6.32	6.76	40.72	6.28	6.89
1d	$(CH_2)_5CO_2H$	$C_8H_{15}NO_2S_2$	B	75	92-93	43.41	6.83	6.33	43.42	6.85	6.33
1e	$(CH_2)_7CO_2H$	$C_{10}H_{19}NO_2S_2$	B	80	67-68	48.16	7.28	5.62	48.13	6.97	5.68
1f	CH_2SO_3K	$C_3H_6KNO_3S_3$	A	30	213-214 dec.	15.05	2.53	5.85	15.02	2.54	5.69
1g	$(CH_2)_2SO_3K$	$C_4H_8KNO_3S_3 \cdot 0.5H_2O$	A	63	234.5-235.5	18.30	3.45	5.33	17.84	3.05	5.39
1h	$(CH_2)_3SO_3K$	$C_5H_{10}KNO_3S_3 \cdot 0.5H_2O$	A	79	291-292	21.72	3.99	5.06	21.39	3.59	4.98
1i	$(CH_2)_5SO_3K$	$C_7H_{14}KNO_3S_3$	A	26	305 dec.	28.45	4.78	4.74	28.31	4.86	4.68
1j	$(CH_2)_2SO_2NH_2$	$C_4H_{10}N_2O_2S_3$	B	91	113-115	22.42	4.70	13.07	22.65	4.67	12.88
1k	$(CH_2)_2SO_2NHC(CH_3)_3$	$C_8H_{18}N_2O_2S_3$	B	90	153-155	35.53	6.71	10.36	35.99	6.84	10.53

(a) Infrared and ^1H nmr spectra supported the assignments of structure. (b) Procedure A used potassium hydroxide as base while procedure B involved triethylamine.

during which time it became pink and then nearly colorless again. Ethanol (100 ml.) was added to the warm reaction mixture. After cooling to room temperature methyl iodide (24.8 ml., 0.40 mole) was added dropwise producing a mild exotherm. The pale green solution was stirred at room temperature for 1.5 hours, and then the ethanol was removed *in vacuo*. Crystals, which formed in the aqueous residue while standing overnight, were collected and washed with ethanol and then sparingly with cold water. Recrystallization from hot ethanol containing 3% water by volume gave **1g** as white crystals (48.0 g.). An additional crop (5.7 g., total yield 53.7 g., 63%) was obtained from the cold water wash (see Table I); ir: 6.65 μ (C=S), 8.4 and 9.45 (SO_2); ^1H nmr (deuterium oxide): δ 2.60 (s, CH_3), 3.27 (t, J = 6.5 Hz, $CH_2SO_3^-$), 4.11 (t, J = 6.5 Hz, NCH_2).

Carboxylic acid analogs made by this procedure were isolated by adjusting the *p*H of the reaction mixture to 2.0 with dilute hydrochloric acid and extracting with ethyl acetate. Evaporation of the ethyl acetate gave oils which crystallized either upon standing, upon trituration with a mixture of hexane and water or from a methanol-water solvent mixture.

Procedure B.

Methyl (2-sulfamoylethyl)carbamodithioate (**1j**).

Carbon disulfide (4.33 ml., 0.072 mole) was added to a solution of 2-aminoethanesulfonamide hydrochloride (11.5 g., 0.072 mole) (9) and triethylamine (19.9 ml., 0.144 mole) in 145 ml. of ethanol. After stirring at room temperature for 2.5 hours, methyl iodide (10.2 g., 0.072 mole) was added dropwise producing an exotherm to 35°. After an additional 2.5 hours of stirring, the ethanol was removed *in vacuo*. The residue was taken up in chloroform and chromatographed on alumina (Fisher A-540) eluting first with chloroform and then 10% methanol in chloroform. The latter eluate gave, upon evaporation *in vacuo*, **1j** as a white solid (14.0 g., 91%). An analytical sample was obtained by recrystallization from water (see Table I); ir: 2.96 and 3.07 μ (NH and NH_2), 6.65 (C=S), 7.76 and 8.69 (SO_2); ^1H nmr (acetone-d_6): δ 2.59 (s, CH_3), 3.43 (t, J = 6.3 Hz, CH_2SO_2), 4.13 (t, J = 6.3 Hz, NCH_2), 7.1 (broad, NH and NH_2).

Carboxylic acid analogs made by this procedure were isolated by evaporating the ethanol, dissolving the residue in water, adding concentrated phosphoric acid to *p*H 1.5 to 2.0 and extracting with ethyl acetate.

Preparation of Dihydrotetrazole-5-thiones.

4,5-Dihydro-5-thioxo-1*H*-tetrazole-1-ethanesulfonic Acid, Compound with Cyclohexanamine (1:2) (**2j**).

A solution of methyl(2-sulfoethyl)carbamodithioate, potassium salt (**1g**) (21.5 g., 0.082 mole) and sodium azide (7.16 g., 0.11 mole) (10) in 200 ml. of water was gently refluxed for 2 hours at which time tlc (7.5 ml. of acetonitrile/2.5 ml. of water plus 3 drops of 3*N* hydrochloric acid on silica gel) indicated the reaction was complete. After cooling to room temperature the reaction mixture was extracted with ether and then passed down a column of strongly acidic Amberlite IR-120H ion-exchange resin. The effluent was extracted with ether and evaporated *in vacuo* to an amber-red oil which was stirred with acetone. After decanting from some insoluble gum, the acetone solution was stripped to dryness *in vacuo*. The residue was dissolved in 2-propanol and treated with cyclohexanamine to *p*H 8-9 (by *p*H paper). Addition of acetonitrile followed by scratching produced **2j** as white crystals (16.0 g., 48%) (see Table II); ir: 3.25-400 μ (with fine structure) (NH_3^+), 8.44 and 9.65 (SO_2); ^1H nmr (deuteriotrifluoroacetic acid): δ 3.88 (t, J = 6.3 Hz, $CH_2SO_3^-$), 4.98 (t, J = 6.3

Table II

Dihydrotetrazole-5-thiones (a)

Compd.	R	Formula	% Yield	M.p., °C	Analyses (%) Calcd. C	H	N	Found C	H	N
2a	CH_2CO_2H	$C_3H_4N_4O_2S$	65	179-180 dec.	22.50	2.52	34.98	22.90	2.71	34.53
2b	$(CH_2)_2CO_2H$	$C_4H_6N_4O_2S$	63	158.5-160.5	27.58	3.47	32.17	27.50	3.48	31.95
2c	$CH(CH_3)CH_2CO_2H$	$C_5H_8N_4O_2S$	50	169-172	31.91	4.28	29.77	32.05	4.35	29.52
2d	$(CH_2)_3CO_2H$	$C_5H_8N_4O_2S$	62	99-101	31.91	4.28	29.77	32.12	4.24	29.86
2e	$(CH_2)_4CO_2H$	$C_6H_{10}N_4O_2S$	40	127-129	35.63	4.98	27.70	35.63	4.98	27.34
2f	$(CH_2)_5CO_2H$	$C_7H_{12}N_4O_2S$	47	100,100.5	38.88	5.59	25.91	38.30	5.51	25.56
2g	$(CH_2)_7CO_2H$	$C_9H_{16}N_4O_2S$	41	94-96	44.25	6.19	22.93	44.16	6.60	22.55
2h	$(CH_2)_{10}CO_2H$	$C_{12}H_{22}N_4O_2S$	23	95-98	50.33	7.74	19.56	50.29	8.02	19.42
2i	CH_2SO_3Na	$C_2H_2N_4Na_2O_3S_2 \cdot 0.5H_2O$	79	293-294 dec.	9.64	1.21	22.48	9.66	1.67	22.09
2j	$(CH_2)_2SO_3H$ (b)	$C_{15}H_{32}N_6O_3S_2 \cdot 2H_2O$	48	167-168.5 dec.	40.52	8.16	18.90	40.42	8.39	18.70
2k	$(CH_2)_3SO_3H$ (b)	$C_{16}H_{34}N_6O_3S_2 \cdot 0.5H_2O$	75	148-151	44.52	7.94	19.47	44.27	7.74	19.11
2l	$(CH_2)_5SO_3Na$	$C_6H_{10}N_4Na_2O_3S_2$	65	287-289 dec.	24.32	3.40	18.91	24.56	3.57	19.10
2m	$(CH_2)_2SO_2NHC(CH_3)_3$	$C_7H_{15}N_5O_2S_2$	71	153-155	31.68	5.70	26.39	31.56	5.62	26.69
2n	$(CH_2)_2SO_2NH_2$ (c)	$C_3H_7N_5O_2S_2$	73	158-162	17.22	3.37	33.47	17.51	3.36	33.16
2o	$(CH_2)_3SO_2NH_2$ (c,d)	$C_4H_9N_5O_2S_2$	48	159-160	21.52	4.06	31.37	21.42	4.03	31.76
2p	CH_2CONH_2 (e)	$C_3H_5N_5OS$	74	219-220 dec.	22.64	3.17	44.00	22.84	2.94	43.62
2q	$CH_2CONHCH_3$ (e)	$C_4H_6N_5NaOS \cdot 2H_2O$	69	126-127	20.77	4.32	30.30	20.46	4.37	29.91
2r	$CH_2CON(CH_3)_2$ (e)	$C_5H_9N_5OS$	72	190-200 dec.	32.08	4.85	37.41	32.35	4.83	37.52
2s	$(CH_2)_2CONH_2$ (f)	$C_4H_7N_5OS$	85	183.5-184.5	27.74	4.07	40.44	27.76	4.00	40.15
2t	$CH(CH_3)CH_2CONH_2$ (f)	$C_5H_9N_5OS$	61	174-175 dec.	32.08	4.85	37.41	32.28	5.05	37.08
2u	$(CH_2)_3CONH_2$ (e)	$C_5H_9N_5OS$	60	133-136	32.08	4.85	37.41	32.00	4.85	37.31
2v	$(CH_2)_5CONH_2$ (f)	$C_7H_{13}N_5OS$	80	155-157	39.06	6.09	32.53	38.98	6.19	32.59
2w	$(CH_2)_{10}CONH_2$ (f)	$C_{12}H_{23}N_5OS$	89	112-114	50.50	8.12	24.54	50.23	8.22	24.46

(a) Infrared and ^1H nmr spectra supported the structure assignments. (b) Compound with cyclohexanamine (1:2). (c) Prepared from the corresponding *N*-(1,1-dimethylethyl)sulfonamides by cleavage with trifluoroacetic acid. (d) Molecular ion confirmed formula. (e) 1,1′-carbonylbis-1*H*-imidazole route. (f) Thionyl chloride route.

Hz, NCH_2) plus peaks for cyclohexanamine.

The disodium salts of other 4,5-dihydro-5-thioxo-1*H*-tetrazole-1-alkanesulfonic acids were prepared by dissolving in methanol the residue from evaporation of the ion-exchange column effluent and treating with 25% sodium methoixde in methanol to *p*H 7.

Carboxylic acid analogs were prepared similarly except one molecular equivalent of sodium hydroxide was included in the reaction mixture to neutralize the carboxylic acid. Workup also differed in that, after cooling, the reaction mixture was adjusted to *p*H 1.5 to 2.0 with dilute hydrochloric acid, and the product was extracted with ethyl acetate. For the preparation of sulfonamide **2m** no sodium hydroxide was required, but use of 50% aqueous ethanol as the solvent was necessary to dissolve carbamodithioate **1k**. Isolation was the same as for the carboxylic acid analogs except that the ethanol was removed *in vacuo* prior to acidification.

Preparation of Carboxamides.

Acid Imidazolide Procedure.

4,5-Dihydro-*N*,*N*-dimethyl-5-thioxo-1*H*-tetrazole-1-acetamide (**2r**).

A solution of 1,1'-carbonylbis-1*H*-imidazole (5.49 g., 0.0339 mole) in 95 ml. of dry THF and 20 ml. of dry DMF was added dropwise, while protected from atmospheric moisture, to a solution of 4,5-dihydro-5-thioxo-1*H*-tetrazole-1-acetic acid (**2a**) (5.42 g., 0.0338 mole) in 75 ml. of dry THF and 20 ml. of dry DMF. After stirring for 35 minutes during which a precipitate formed, dry THF (250 ml.) saturated with *N*-methylmethanamine was added, and complete solution returned. The reaction mixture was concentrated *in vacuo* to 200 ml., and a large volume of ether was added to precipitate a gummy solid. An aqueous solution (170 ml.) of this solid was adjusted to *p*H 2.0 with 6*N* sulfuric acid and extracted with ethyl acetate. The extract was dried over magnesium sulfate and evaporated *in vacuo* to give a residue which upon trituration with a mixture of 10 ml. of ethyl acetate and 200 ml. of ether gave **2r** as a pale yellow solid (4.57 g., 72%) (see Table II); ir: 3.28 μ (NH), 6.05 (C=O), 6.64 (C=S); ^{1}H nmr (DMSO-d_6): δ 2.90 and 3.11 [$N(CH_3)_2$], 5.30 (CH_2).

Acid Chloride Procedure.

4,5-Dihydro-5-thioxo-1*H*-tetrazole-1-propanamide (**2s**).

A suspension of 4,5-dihydro-5-thioxo-1*H*-tetrazole-1-propanoic acid (**2b**) (74.5 g., 0.428 mole) in 200 ml. of thionyl chloride protected from moisture by calcium sulfate was warmed at 50° until solution was complete and evolution of gas had ceased (*ca.* 2.5 hours). Excess thionyl chloride was evaporated *in vacuo* to leave 4,5-dihydro-5-thioxo-1*H*-tetrazole-1-propanoyl chloride as a viscous amber oil (82.3 g., ~100%).

The acid chloride was dissolved in 250 ml. of dry THF and added dropwise over 20 minutes to 600 ml. of concentrated aqueous ammonium hydroxide at 0°. After stirring 0.5 hour in the cold and 1 hour at room temperature, the reaction mixture was concentrated *in vacuo* to about 300 ml. Addition of 6*N* sulfuric acid to drop the *p*H from 5.2 to 2.5 and ice-cooling produced a solid which was washed with water and recrystallized from ethanol to give **2s** (61.6 g., 85%) (see Table II); ir: 3.00, 3.16 and 6.22 μ (NH_2), 6.01 (C=O), 6.63 (C=S); ^{1}H nmr (acetone-d_6): δ 2.84 (t, J = 6.5 Hz, CH_2CO), 4.48 (t, J = 6.5 Hz, NCH_2), 6.0-8.3 (NH and NH_2).

Dihydro-2*H*-1,2,4-thiadiazine-3(4*H*)thione, 1,1-Dioxide (**3**).

Methyl (2-sulfamoylethyl)carbamodithioate (**1j**) (0.90 g., 4.2 mmoles) and sodium azide (0.60 g., 9.3 mmoles) in 20 ml. of water were heated at 78° for 2.5 hours. The reaction mixture was cooled and filtered, and the filtrate was extracted with ethyl acetate. The aqueous fraction was treated with dilute hydrochloric acid to *p*H 2.0, saturated with sodium chloride and extracted with ethyl acetate. The extract was dried over magnesium sulfate and stripped to dryness *in vacuo*. The residue was triturated with ethyl acetate to give **3** (0.40 g., 57%). An analytical sample was obtained by crystallization from a mixture of acetone and chloroform; m.p. 200-202° dec.; ir: 3.18 μ (NH), 6.40 (C=S), 7.53 and 8.85 (SO_2); ^{1}H nmr (DMSO-d_6): δ 4.64 (s, broad, CH_2CH_2), 6.89-7.27 (m, broad, NH).

Anal. Calcd. for $C_3H_6N_2O_2S_2$: C, 21.68; H, 3.64; N, 16.85. Found: C, 21.83; H, 3.61; N, 16.49.

2-(1,3-Dihydro-1,3-dioxo-2*H*-isoindol-2-yl)-*N*-(1,1-dimethylethyl)-ethanesulfonamide.

A solution of 2-(1,3-dihydro-1,3-dioxo-2*H*-isoindol-2-yl)ethanesulfonyl chloride (76.4 g., 0.28 mole) (9) in 600 ml. of dry chloroform was added dropwise over 15 minutes to a solution of 2-methyl-2-propanamine (61.4 g., 0.84 mole) in 600 ml. of dry chloroform at 5°. After stirring for 3 hours at room temperature, insoluble material was filtered off, and the filtrate was applied to a silica gel column. The column was eluted with first chloroform and then 5% methanol in chloroform. Evaporation *in vacuo* of the eluate gave the title compound as a cream-colored solid (72.4 g., 83%), m.p. 151-155°; ir: 3.05 μ (NH), 5.64 and 5.84 (C=O), 7.65 and 8.79 (SO_2); ^{1}H nmr (deuteriochloroform): δ 1.37 (s, $C(CH_3)_3$), 3.35 (t, J = 6.3 Hz, CH_2SO_2), 4.12 (t, J = 6.3 Hz, NCH_2), 4.72 (s, NH), 7.75 (m, aromatic H).

Anal. Calcd. for $C_{14}H_{18}N_2O_4S$: C, 54.18; H, 5.85; N, 9.03; S, 10.33. Found: C, 53.84; H, 5.84; N, 9.03; S, 10.33.

2-Amino-*N*-(1,1-dimethylethyl)ethanesulfonamide, Hydrochloride (**4**).

A mixture of 2-(1,3-dihydro-1,3-dioxo-2*H*-isoindol-2-yl)-*N*-(1,1-dimethylethyl)ethanesulfonamide (72.4 g., 0.234 mole) and hydrazine hydrate (11.85 g., 0.237 mole) in 700 ml. of 95% ethanol was heated at reflux for 3 hours. The ethanol was stripped off *in vacuo*, and the resulting solid was suspended in 1500 ml. of water. Dilute hydrochloric acid was added to bring the *p*H to 3.0, and after stirring 10 minutes, the insoluble material was removed by filtration. The aqueous solution was stripped to dryness, and a benzene azeotrope was used to remove the last traces of moisture giving **4** as a solid (40.4 g., 80%). Crystallization from chloroform gave an analytical sample, m.p. 138-140°; ir: 2.91, 3.00 and 3.17 μ (NH), 3.79-4.20 (with fine structure), 6.25, 6.33 and 6.62 (NH_3+), 7.64 and 8.86 (SO_2); ^{1}H nmr (deuterium oxide): δ 1.40 (s, $C(CH_3)_3$), 3.58 (multiplet, CH_2CH_2).

Anal. Calcd. for $C_6H_{17}ClN_2O_2S$: C, 33.25; H, 7.91; N, 12.93. Found: C, 33.22; H, 8.10; N, 13.03.

4,5-Dihydro-5-thioxo-1*H*-tetrazole-1-ethanesulfonamide (**2n**).

A solution of *N*-(1,1-dimethylethyl)-4,5-dihydro-5-thioxo-1*H*-tetrazole-1-ethanesulfonamide (**2m**) (199 g., 0.75 mole) in 1.0 l. anisole and 2.0 l. trifluoroacetic acid was refluxed for 1.2 hours. Upon cooling a white solid formed which was collected. Addition of petroleum ether (b.p. 35-60°) to the filtrate produced additional solid **2n** (a total of 115.2 g., 73%) (see Table II); ir: 3.04 and 3.18 μ (NH_2), 6.63 (C=S), 8.74 (SO_2); ^{1}H nmr (acetone-d_6): δ 3.72 (t, J = 6.5 Hz, CH_2SO_2), 4.81 (t, J = 6.5 Hz, NCH_2), 6.40 (broad, NH_2).

Acknowledgment.

We gratefully acknowledge Drs. Francis R. Pfeiffer and John G. Gleason, Ms. Sylvia Fagan and Messrs. Stanley J. Schmidt, Charles M. Kinzig, Thomas F. Buckley III and Larry D. Davis for the synthesis of selected compounds. We also wish to thank Dr. John

R. E. Hoover for his advice and support and Miss Edith Reich and her staff in the Analytical and Physical Chemistry Department of Smith Kline and French Laboratories for the elemental analyses.

REFERENCES AND NOTES

(1a) R. Stollé and F. Henke-Stark, *J. Prakt. Chem.*, **124**, 261 (1930); (b) E. Lieber and J. Ramachandran, *Can. J. Chem.*, **37**, 101 (1959).

(2) R. E. Orth and J. W. Jones, *J. Pharm. Sci.*, **51**, 862 (1962).

(3) E. Lippmann, H. Loester and A. Antonowa, *J. Signalaufzeichnungsmaterialien*, **2**, 209 (1974).

(4) E. Lieber, C. N. Pillai and R. D. Hites, *Can. J. Chem.*, **35**, 832 (1957).

(5) The recently reported synthesis of carbamodithioates by the reaction of trithiocarbonate *SS*-dioxides with amines represents another possible method of preparation, see N. H. Nilsson, C. Jacobsen and A. Senning, *J. Chem. Soc., Chem. Commun.*, 314 (1971).

(6a) H. Körner, *Chem. Ber.*, **41**, 1901 (1908); (b) P. Aubert, E. B. Knott and L. A. Williams, *J. Chem. Soc.*, 2185 (1951); (c) S. Yamada, K. Ishikawa and K. Achiwa, *Chem. Pharm. Bull.*, **19**, 912 (1971).

(7) G. C. Barrett and C. M. O. A. Martins, *J. Chem. Soc., Chem. Commun.*, 638 (1972).

(8) Anisole was included to scavenge 1,1-dimethylethyl cations.

(9) R. Winterbottom, J. W. Clapp, W. H. Miller, J. P. English and R. O. Roblin, Jr., *J. Am. Chem. Soc.*, **69**, 1393 (1947).

(10) To minimize the amount of sodium azide used and thus the amount of dangerous hydrazoic acid generated during workup, an alternate procedure was used in some later preparations. Initially, equimolar amounts of carbamodithioate and sodium azide were employed, but if tlc monitoring indicated that conversion to product had essentially stopped and carbamodithioate still remained, additional small amounts of sodium azide were added until no more carbamodithioate was left.