TABLE III
$ArSO_2OCH_2C{\equiv}CCH_2OSO_2Ar$

No.	Ar	Method of prepn[a]	Yield, %	Recrystn solvent[b]	Mp, °C	Formula	Calcd, % C	Calcd, % H	Found, % C	Found, % H
VII	2,5-Dimethylphenyl	D	29	G	104–105	$C_{26}H_{22}O_6S_2$	56.85	5.25	56.91	5.25
VIII	2,5-Dichlorophenyl	D	81	E	137–139	$C_{16}H_{10}Cl_4O_6S_2$	38.11	2.00	37.94	2.01
IX	*p*-Nitrophenyl	D	33	E	178–180	$C_{16}H_{12}N_2O_{10}S_2$	42.10	2.65	42.31	2.84
X	2,4-Dimethylphenyl	D	36	E	105–107	$C_{26}H_{22}O_6S_2$	56.85	5.25	57.03	5.19
XI	3,4-Dichlorophenyl	D	81	H	105–107	$C_{16}H_{10}Cl_4O_6S_2$	38.11	2.00	38.30	2.07
XII	2,5-Dibromophenyl	D	81	E	114–118	$C_{16}H_{10}Br_4O_6S_2$	28.19	1.46	28.53	1.49
XIII	4-Chloro-3-nitrophenyl	D	39	E	116–117	$C_{16}H_{10}Cl_2N_2O_{10}S_2$	36.52	2.06	36.70	2.08
XIV	Thienyl	D	66	G	96–97	$C_{12}H_{10}O_6S_4$	37.10	2.65	37.22	2.73
XV	*m*-Nitrophenyl	D	23	E	127–128.5	$C_{16}H_{12}N_2O_{10}S_2$	42.10	2.65	41.93	2.49
XVI	*p*-Bromophenyl	D	49	E	135–137	$C_{16}H_{12}Br_2O_6S_2$	36.65	2.09	36.58	2.18

[a] See Experimental Section. [b] E = acetone, G = acetone–H_2O (3:2), H = petroleum ether (bp 60–110°).

Preparation of Arylsulfonic Acid Esters of 1,4-But-2-ynediol. Method D.—The 1,4-but-2-ynediol bis(arylsulfonates) (VII–XVI, Table III) were prepared by a procedure similar to that described by Eglington and Whitling.[17] A solution of 0.101 mole of KOH in 10 ml of water at 0° was added to 40 ml of acetonitrile at 10–20°, containing 0.10 mole of arylsulfonyl chloride and 0.05 mole of 1,4-but-2-ynediol. The addition took 30 min. The solution was then stirred at room temperature for 2–4 hr. The material precipitated was collected by vacuum filtration. The solid was air dried and then extracted with boiling acetone. Good to excellent yields of the esters recrystallize from the acetone solutions upon cooling to 0°.

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(17) G. Eglington and W. C. Whitling, *J. Chem. Soc.*, 3651 (1950).

Synthesis of N-Monosubstituted 2-Mercaptoethylamines with Thioureido Substituents[1,2]

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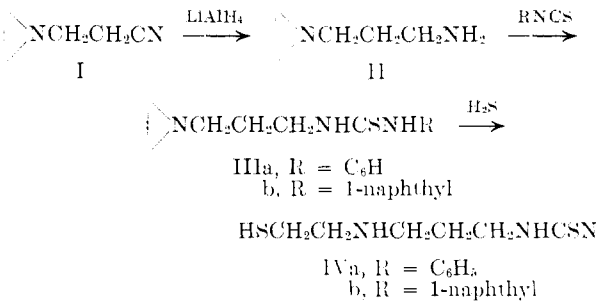
Because of the interest in 2-mercaptoethylamines and their derivatives as potential antiradiation drugs,[3-7] and the fact that certain 1-alkyl-3-(2-mercaptoethyl)-thioureas[8] were found to be effective radiation-protective agents,[9] we have synthesized a few N-monosubstituted 2-mercaptoethylamines, $RNHCH_2CH_2SH$, in which the R group includes thioureido. The method is shown in Scheme I. Data on the compounds with

SCHEME I



structures III and IV are presented in Tables I and II, respectively.

Both compounds were tested at 51–150 mg/kg ip in mice for 30-day survival against lethal radiation of 1000 r.[10] Neither of the amino mercaptans bearing the thioureido group provided mice any protection against lethal doses of radiation.

Experimental Section[11]

N-(3-Aminopropyl)ethylenimine.—A solution of 20.0 g (0.21 mole) of β-ethyleniminopropionitrile[12] in 40 ml of dry ether was added dropwise to a slurry of 7.9 g (0.21 mole) of $LiAlH_4$ in 200 ml of dry ether at 0° with stirring in a nitrogen atmosphere. The resultant reaction mixture was stirred at 0° for 30 min. Then, at 0°, 8 ml of water, 6 ml of 20% NaOH, and 28 ml of water were cautiously added in that order. The granular white solids formed in this way were removed by suction filtration, then washed with ether. The ethereal solutions were combined, dried ($MgSO_4$), and then concentrated by distillation through a Vigreux column. The residue obtained was distilled *in vacuo* and gave 6.3 g (30%) of product, bp 67–69° (27 mm), $n^{23}D$ 1.4567. Bestian[12] gives bp 61–62° (19 mm) for the compound prepared by catalytic hydrogenation.

Anal. Calcd for $C_5H_{12}N_2$: C, 59.95; H, 12.08; N, 27.97. Found: C, 59.75; H, 12.11; N, 27.76.

1-(3-Ethyleniminopropyl)-3-(1-naphthyl)thiourea.—1-Naphthyl isothiocyanate (4.6 g, 0.025 mole) and N-(3-aminopropyl)-ethylenimine (2.5 g, 0.025 mole) were dissolved in reagent grade benzene, heated to boiling, and cooled. A white solid, 4.7 g (66%), mp 128–131°, precipitated and was collected by suction on

(1) This work was supported by the U. S. Army Medical Research and Development Command, Department of the Army, under Contract No. DA-49-193-2174.

(2) This is the second paper dealing with the synthesis of N-monosubstituted 2-mercaptoethylamines. For the preceding paper see A. F. Ferris, O. L. Salerni, and B. A. Schutz, *J. Med. Chem.*, **9**, 391 (1966).

(3) *Cf.* Symposium on Radiation-Protective Agents, 141st National Meeting of the American Chemical Society, Washington, D. C., March 1962.

(4) D. D. Reynolds, D. L. Fields, and D. L. Johnson, *J. Org. Chem.*, **26**, 5130 (1961).

(5) R. J. Wineman, M. H. Gelbs, J. C. James, and A. M. Pomponi, *ibid.*, **27**, 4222 (1962).

(6) F. I. Carroll, H. M. Dickson, and M. E. Wall, *ibid.*, **30**, 33 (1965).

(7) D. Rosenthal, G. Brandrup, K. H. Davis, Jr., and M. E. Wall, *ibid.*, **30**, 3689 (1965).

(8) A. F. Ferris and B. A. Schutz, *ibid.*, **28**, 3140 (1963).

(9) Test data supplied by Walter Reed Army Institute of Research, Washington, D. C.

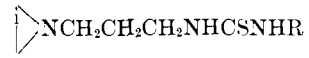
(10) L. Field, A. Ferrari, R. Creilsbaw, and T. Owen, *J. Med. Chem.*, **7**, 42 (1964).

(11) Melting points are corrected and the boiling point is uncorrected. Microanalyses were performed by Galbraith Laboratories, Knoxville, Tenn. Infrared spectra were recorded on a Perkin-Elmer Model 137 Infracord spectrophotometer.

(12) H. Bestian, *Ann.*, **556**, 210 (1950).

TABLE I

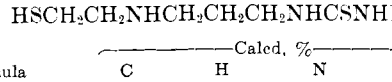
1-(3-ETHYLENIMINOPROPYL)-3-SUBSTITUTED THIOUREAS



R	Yield, %	Mp, °C	Recrystn solvent	Calcd, % C	H	N	S	Found, % C	H	N	S
C_6H_5	72	107–109	Ethyl acetate	61.24	7.28	17.85	13.63	61.36	7.20	17.92	13.79
$C_{10}H_7$	66	129.5–130.5	Benzene	67.33	6.71	14.72	11.23	67.54	6.64	14.59	11.41

TABLE II

1-[3-(2-MERCAPTOETHYLAMINO)PROPYL]-3-SUBSTITUTED THIOUREAS



R	Yield, %	Mp, °C	Formula	Calcd, % C	H	N	S	Found, % C	H	N	S
C_6H_5	100	77–79.5	$C_{12}H_{19}N_3S_2$	53.49	7.10	15.60	23.80	53.62	7.10	15.51	23.80
$C_{10}H_7$	100	106–108	$C_{16}H_{21}N_3S_2$	60.15	6.30	13.15	20.07	60.13	6.38	13.09	20.29

filtration. After a recrystallization from benzene, an analytical sample of 1-(3-ethyleniminopropyl)-3-(1-naphthyl)thiourea was obtained, mp 129.5–130.5°.

1-[3-(2-Mercaptoethylamino)propyl]-3-phenylthiourea.—Hydrogen sulfide was bubbled into absolute ethanol at −60° for 1 hr; approximately 12.0 g of H_2S was absorbed. This solution was cautiously added to 2.5 g (0.01 mole) of analytically pure 1-(3-ethyleniminopropyl)-3-phenylthiourea dissolved in 150 ml of a 1:1 mixture of chloroform and anhydrous ethanol. The solution was allowed to stand for 3 hr, then additional hydrogen sulfide was bubbled through the solution for 15 min. The solution was concentrated *in vacuo* on a rotary evaporator to afford a clear oil which, on rubbing with a glass rod, gave 2.5 g (quantitative yield) of snow white solid, mp 77.5–80°. The infrared spectrum showed a mercaptan peak at 2550 cm^{-1}.[13]

(13) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1958, p 350.

Some Bridgehead-Substituted Tetrahydroacenaphthenones[1a]

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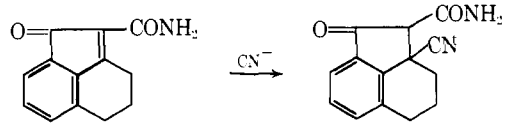
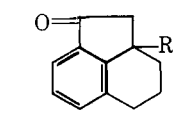
Attention has recently been called to the importance of rigid molecules, commonly possessing quaternary or bridgehead carbon atoms, in developing biologically active molecules of high potency.[2] A series of 2-dialkylaminoalkyl-2a,3,4,5-tetrahydroacenaphthen-1-ones has been reported,[3] some of which had analgesic activity. The ready availability of 2-carboxamido-2a-cyano-2a,3,4,5-tetrahydroacenaphthen-1-one (**2**),[4] *via* the Michael addition of cyanide ion to 2-carboxamido-3,4-trimethyleno-1-indenone (**1**),[5] led to the preparation of several tetrahydroacenaphthene derivatives of **2** for pharmacological screening. These compounds are rigid molecules containing a quaternary carbon atom at a bridgehead, and hence might have enhanced biological activity.

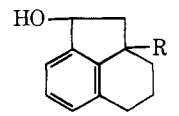


1 2

Hydrolysis of **2** with aqueous sulfuric acid (5–35%) led to 2a-carboxy-2a,3,4,5-tetrahydroacenaphthen-1-one (**3a**), while hydrolysis using 20% phosphoric acid gave a mixture of 2a-cyano-2a,3,4,5-tetrahydroacenaphthen-1-one (**3b**) and **3a**. The structure of **3a** is indicated by its stability (not a β-keto acid) and by the hydrolysis of **3b** with 50% aqueous sulfuric acid to a keto acid shown to be identical with **3a**. The acid **3a** was converted to β-diethylaminoethyl (**3c**), γ-dimethylaminopropyl (**3d**), and β-1-piperidinoethyl 1-oxo-2a-3,4,5-tetrahydroacenaphthene-2a-carboxylate hydrochloride (**3e**) by treatment with the appropriate dialkylaminoalkyl chloride hydrochloride and potassium carbonate in dimethylformamide. Treating the acid chloride of **3a** with the appropriate alcohol led to the formation of **3c** and **3d**. β-Chloroethyl 1-oxo-2a,3,4,5-tetrahydroacenaphthene-2a-carboxylate (**3f**) was formed when a mixture of **3a**, ethylene chlorohydrin, and concentrated sulfuric acid was heated in benzene. Treatment of **3b** with concentrated sulfuric acid af-



3a, R = CO_2H
b, R = CN
c, R = $CO_2CH_2CH_2N(C_2H_5)_2 \cdot HCl$
d, R = $CO_2(CH_2)_3N(CH_3)_2 \cdot HCl$
e, R = $CO_2CH_2CH_2N(CH_2)_5 \cdot HCl$
f, R = CH_2CH_2Cl
g, R = $CONH_2$



4a, R = CO_2H
b, R = CN
c, R = $CO_2CH_2CH_2N(C_2H_5)_2 \cdot HCl$

(1) (a) Contribution No. 1391. This work was supported by a grant from the Bristol Laboratories, Division of Bristol-Myers Co., Syracuse, N. Y., and is taken in part from theses submitted to Indiana University for the degree Doctor of Philosophy by W. L. Roelofs, June 1964, and by R. F. Weddleton, June 1965. Presented in part before the Division of Medicinal Chemistry, 148th National Meeting of the American Chemical Society, Detroit, Mich., April 1965. (b) Bristol Laboratories Predoctoral Fellow, 1962. (c) Bristol Laboratories Predoctoral Fellow, 1962–1965.

(2) E. L. May, *J. Med. Chem.*, **6**, 322 (1963); L. H. Sarett, Award Address for Creative Work in Synthetic Organic Chemistry, 147th National Meeting of the American Chemical Society, Philadelphia, Pa., April 1964.

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