Anal. Calcd. for $C_7H_6N_6O$: C, 44.21; H, 3.18; N, 44.20. Found: C, 44.27; H, 3.07; N, 44.08.

A dinitrophenylhydrazone was prepared for analysis.

Anal. Calcd. for $C_{13}H_{10}N_{10}O_4 \cdot 3H_2O$: C, 36.80; H, 3.80; N, 32.99. Found: C, 36.98; H, 3.39; N, 33.20.

The ultraviolet absorption characteristics of 2,4-diamino-6-pteridinecarboxaldehyde are: in 0.1 *N* HCl, λ_{max} 244 mμ (log ϵ 4.16), 262 infl (3.86), 334 (4.04); in 0.1 *N* NaOH, λ_{max} 225 mμ (log ϵ 4.02), 257 (4.27), 275 infl (4.00), and 372 (3.93).

Isolation of 3,5-Diiodo-4-aminobenzoylglutamic Acid.—Fraction B mentioned above was concentrated at room temperature until a brown sirup was obtained. It was dissolved in 5 ml. of 0.1 *N* NaOH, warmed with a little Darco G-60, and filtered. Acidification of the filtrate caused the separation of a brownish oil. The aqueous phase was decanted and the oil, after washing with water and triturating with 10 ml. of methanol, slowly crystallized. The crystalline material was collected and washed with ethyl acetate. The yield was 0.1 g. (5%), m.p. 220° dec. An analytical sample was prepared by dissolving the brownish crystals in dilute NaOH and reprecipitation with a few drops of glacial acetic acid. Repetition of this procedure afforded a colorless crystalline material, m.p. 222–224° dec. undepressed by an authentic sample of 3,5-diiodo-4-aminobenzoylglutamic acid.[8]

Anal. Calcd. for $C_{12}H_{12}I_2N_2O_5$: C, 27.82; H, 2.34; I, 48.99; N, 5.41. Found: C, 27.78; H, 2.50; I, 49.09; N, 5.45.

Oxidative Degradation of 3′-Iodoaminopterin.—3′-Iodoaminopterin (100 mg.) was dissolved in 5 ml. of 0.1 *N* NaOH and heated in a water bath at 90°. The solution was stirred vigorously and to it was slowly added 1 ml. of 5% $KMnO_4$ in 5 min. The mixture was cooled to room temperature and filtered. The precipitate was washed with a little dilute NaOH then water. The combined filtrate and washings were acidified with 0.5 ml. of glacial acetic acid, and the yellow precipitate (fraction A) was separated from the supernatant (fraction B) by filtration.

Fraction A.—The yellow precipitate was stirred twice with 5 ml. each of 0.1 *M* phosphate buffer of pH 8, and the yellow solution was discarded. The insoluble material was dissolved in 5 ml. of 0.1 *N* NaOH and filtered. The filtrate was acidified with a few drops of glacial acetic acid and centrifuged. The yellow gelatinous material weighed 30 mg. and showed ultraviolet absorption spectra identical with authentic 2,4-diamino-6-pteridinecarboxylic acid.[17]

Anal. Calcd. for $C_7H_6N_6O_2 \cdot H_2O$: C, 37.50; H, 3.60. Found: C, 37.39; H, 3.72.

Fraction B.—The supernatant was further acidified with 1 ml. of concentrated HCl and extracted four times with 10 ml. of ethyl acetate each time. The combined extract was concentrated in a stream of nitrogen at 90° after drying ($MgSO_4$). The yellowish oil was taken up in 1 ml. of ethyl acetate. Upon addition of a few drops of petroleum ether (b.p. 30–60°), yellowish crystals began to form. These crystals were collected and washed with a small volume of ethyl acetate; yield 30 mg., m.p. 164–168°. The product was identical spectrally and chromatographically with an authentic sample of **3-iodo-4-aminobenzoylglutamic acid** prepared according to the following procedure.

Anal. Calcd. for $C_{12}H_{13}IN_2O_5$: C, 36.75; H, 3.34; N, 7.14. Found: C, 36.48; H, 3.32; N, 7.07.

3-Iodo-4-aminobenzoylglutamic Acid.—A mixture of *p*-aminobenzoylglutamic acid (1.07 g., 4 mmoles), iodine (1.12 g., 4.4 mmoles),[23] and 20 ml. of dimethylformamide were placed in a conical flask, wrapped in aluminum foil, and vigorously stirred at room temperature for 5 days. The mixture was concentrated at room temperature in a stream of air. The sirupy residue was taken up in 20 ml. of 1 *N* HCl and extracted with one 20-ml. portion and three 10-ml. portions of ethyl acetate. The combined extract was washed with 20 ml. of 1% KI, then with 25 ml. of 20% sodium thiosulfate. After being dried ($MgSO_4$), the ethyl acetate extract was concentrated in nitrogen at 90°. The resultant oil slowly crystallized. It was triturated with 5 ml. of petroleum ether (b.p. 66–75°) and 5 ml. of ethyl acetate, filtered, and finally washed with ethyl acetate; yield 0.6 g. (39%), m.p. 168°.

Anal. Calcd. for $C_{12}H_{13}IN_2O_5$: C, 36.75; H, 3.34; I, 32.36; N, 7.14. Found: C, 36.89; H, 3.27; I, 32.06; N, 7.12.

(23) A larger excess of iodine resulted in the formation of the 3,5-diiodo compound in addition to the monoiodo compound.

When chromatographed on Whatman 3 mm. paper and developed with 0.1 *M* acetate buffer of pH 4.4, ascending flow, it had R_f 0.74 (observed under ultraviolet light of 254 mμ). The ultraviolet absorption characteristics were: in 0.1 *N* NaOH, λ_{max} 226 mμ (log ϵ 4.30), 272 (4.11); in 0.1 *N* HCl, λ_{max} 220 mμ (log ϵ 4.29), 275 (3.85).

Bis(2-chloroalkyl)amides of Acylated Amino Acids. Modified Nitrogen Mustards[1]

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A considerable number of aliphatic and aromatic compounds carrying an N,N-bis(2-chloroethyl)amino group (nor-nitrogen mustards) have been investigated in the search for antitumor agents.[2] The effective dose of these compounds, however, is in many cases so close to the dose which produces serious toxic effects in the host as to render them unsuitable for prolonged chemotherapeutic use. Many workers have, therefore, sought nor-nitrogen mustard derivatives possessing the high carcinolytic activity of the parent compound but having a greatly reduced general toxicity.[3] A few of these alkylating agents are in clinical use today.[4]

We have converted the basic nitrogen atom to the relatively neutral amide nitrogen by synthesizing bis(2-chloroethyl)amides and bis(2-chloropropyl)amides of N-acylated amino acids, thus hindering formation of the reactive aziridinium intermediate. The cytotoxic nor-nitrogen mustard might then be liberated by action of proteolytic enzymes in cancer cells, resulting in a possible selectivity of antitumor action. Safonova and Sergievskaya as well as Bien and Friedman reported the preparation of glycinebis(2-chloroethyl)-amide.[5]

All of these N-acylated-α-amino acid "nitrogen mustard" amides listed in Table I were prepared in essentially the same manner from the N-acylated amino acid and the di(2-chloroalkyl)amine in the presence of

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TABLE I

BIS(2-CHLOROALKYL)AMIDES OF ACYLATED AMINO ACIDS

Compd.	R	R′	Method of prepn.	M.p., °C.	Yield, %	Formula	% C Calcd.	% C Found	% H Calcd.	% H Found	% N Calcd.	% N Found	Infrared band, cm.$^{-1}$[a]
						$RCHCON(CH_2CH_2Cl)_2$							
						NHCOR′							
I	H	CH_3	A	100–102	27.6	$C_8H_{16}Cl_2N_2O_2$	39.85	40.83	5.85	6.04	11.62	11.15	1628
II	H	$CHCl_2$	A	62.5–63.5	38.5	$C_8H_{12}Cl_4N_2O_2$	30.99	30.87	3.90	4.06	9.04	9.10	1631
III	H	C_6H_5	B	92–94	55.0	$C_{13}H_{16}Cl_2N_2O_2$	51.50	52.43[b]	5.32	5.42	9.24	9.09	1629
IV	CH_3	CH_3	A	85–86	46.2	$C_9H_{16}Cl_2N_2O_2$	42.36	42.88	6.32	6.45	10.98	10.78	1629
V	CH_3	$CHCl_2$	B	117.5–119	23.5	$C_9H_{14}Cl_4N_2O_2$	33.36	33.69	4.35	4.54	8.65	8.41	1631
VI	CH_3	C_6H_5	B	96–97	34.0	$C_{14}H_{18}Cl_2N_2O_2$	53.01	53.59	5.72	5.76	8.83	8.48	1626
VII	$C_6H_5CH_2$	CH_3	A or B	119–121	51.0	$C_{15}H_{20}Cl_2N_2O_2$	54.39	54.15	6.09	6.21	8.45	8.33	1629
VIII	$C_6H_5CH_2$	$CHCl_2$	A	147–148	47.6	$C_{15}H_{18}Cl_4N_2O_2$	45.02	44.78	4.53	4.81	7.00	6.98	1615
IX	$C_6H_5CH_2$	C_6H_5	B	133–135	27.7	$C_{20}H_{22}Cl_2N_2O_2$	61.07	61.04	5.64	5.83	7.12	7.07	1628
X	$(CH_3)_2CH$	CH_3	A	95–96	43.3	$C_{11}H_{20}Cl_2N_2O_2$	46.65	46.82	7.12	7.13	9.89	9.72	1630
XI	$(CH_3)_2CHCH_2$	CH_3	A	92–93	26.2	$C_{12}H_{22}Cl_2N_2O_2$	48.49	48.86	7.46	7.58	9.42	9.26	1634
XII	CH_3OCH_2	$CHCl_2$	B	84–85	56.5	$C_{10}H_{16}Cl_4N_2O_3$	33.92	33.82	4.56	4.49	7.91	7.75	1622
XIII	$CH_3SCH_2CH_2$	$CHCl_2$	A	82.5–84	26.5	$C_{11}H_{18}Cl_4N_2O_2S$	34.39	35.05[b]	4.72	4.89	7.29	7.03	1632
XIV	$CH_3SCH_2CH_2$	CH_3	B	81–82	22.2	$C_{11}H_{20}Cl_2N_2O_2S$	41.90	42.38	6.39	6.43	8.89	8.79	1631
XV	$C_6H_5CH_2$	CCl_3	A	118	41.2	$C_{15}H_{17}Cl_5N_2O_2$	41.45	42.16	3.94	4.04	6.45	6.28	1637
						$RCHCON(CH_2CHClCH_3)_2$							
						NHCOR′							
XVI	$C_6H_5CH_2$	$CHCl_2$	A	122–123	42.6	$C_{17}H_{22}Cl_4N_2O_2$	47.68	48.38	5.18	5.36	6.54	6.42	1620
XVII	CH_3	CH_3	A	108–110	24.7	$C_{11}H_{20}Cl_2N_2O_2$	46.65	47.11	7.12	7.30	9.89	9.71	1625

[a] L. J. Bellamy ("Infrared Spectra of Complex Molecules," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1958, p. 205) gives a range of 1670–1630 cm.$^{-1}$ for tertiary amides. [b] This product is rather labile and all attempts to date to purify it by crystallization resulted in some decomposition. The product reported here was obtained directly from the ethyl acetate solution of the reaction.

dicyclohexylcarbodiimide by the method of Sheehan.[6] The reactions set in almost immediately on mixing tetrahydrofuran solutions of the reactants at room temperature. In general, no attempt was made to control the slight rise in temperature which occurred. The yield of N,N′-dicyclohexylurea, formed as an insoluble by-product, was practically quantitative in each case. There were minor variations in the product recovery procedures, as described in the Experimental section. The products were obtained in crystalline form in yields of 23 to 56%. Many of the compounds tended to rearrange to esters[3e,5] during recrystallization. Other changes also appear to take place, and these are under investigation. Some of the analyses were, therefore, carried out on the crude products as obtained from the reaction mixture. The tertiary amide bonds were identified by infrared absorption spectra. N-Acylated amino acids were employed because a number of attempts to prepare the amides directly from nonacylated amino acids were unsuccessful, yielding unreacted amino acid or impure unidentified sirups. Free α-amino acids do not represent suitable starting materials because of their zwitterion structure.

The modified nitrogen mustards were tested for inhibition of Sarcoma 180 (S180) *in vivo;* several were also tested against Carcinoma 1025 (C1025). Although bis(2-chloroethyl)methylamine (HN2) is known to exert little effect upon S180, some derivatives of it, as well as other alkylating agents, have marked inhibitory effects on this tumor.[7] Carcinoma 1025, on the other hand, is significantly inhibited by most alkylating agents, including HN2.[7]

Mice bearing either S180 or C1025 tolerated relatively high doses of all the compounds (Table II). Only two compounds, XII and XV, exhibited any inhibitory effects upon the growth of S180. When treatment was begun 5 days after implantation of tumor, significant inhibition of C1025 was demonstrated at the end of treatment with six of the ten compounds tested. Results from other tests in which treatment was begun 24 hr. after implantation of C1025 were similar. Observed inhibitory effects upon C1025 persisted for at least 1 week after cessation of treatment. Inhibitory effects, even the minimal ones observed with S180, were achieved only at dose levels toxic to the host, as evidenced by some deaths and excessive losses in body weight.

Compounds VI, X, XI, XV, and XVI were tested also against the ascitic form of Ehrlich carcinoma. Compounds VI, X, and XI induced significant retardation of neoplastic development at doses of 500 mg./kg./day but not at 250 mg./kg./day. Inhibitory effects of VI and X were achieved without toxicity to the host, whereas the effective dose of XI resulted in 50% mortality among the test animals. Compounds XV and XVI at 1000 mg./kg./day, causing rather severe losses in body weight of the host, exerted no effects upon the development of ascites. Compound X at maximally tolerated doses had no inhibitory effects upon carcinoma E0771, sarcoma T241, or Ridgway osteogenic sarcoma.

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Experimental

The melting points were obtained with a Fisher-Johns apparatus and are uncorrected. Infrared spectra were determined

TABLE II

EFFECTS OF BIS(2-CHLOROALKYL)AMIDES OF ACYLATED AMINO ACIDS UPON THE GROWTH OF SARCOMA 180 AND CARCINOMA 1025 *in Vivo*.

		Sarcoma 180			Carcinoma 1025			
		Tumor[b]	AWC[c]	Mor-	Tumor[b]		AWC[c]	Mor-
Compd.[a]	Dose, mg./kg./day	*T/C*	*T/C*	tality[d]	*T/C*	Effect	*T/C*	tality[d]
I	250[e]	1.04	−0.5/+0.5	0/5				
II	500				0.60	+	−2.5/−0.8	1/10
	250				0.65	−	−2.7/−0.1	0/5
	62.5	0.86	−1.5/+0.5	0/5				
III	500	0.85	+1.5/+1.0	1/5				
IV	500	0.86	−4.0/+0.5	2/5		Toxic		5/5
	250				0.80	−	−2.1/−0.8	1/10
V	500	0.86	−2.0/+0.5	0/5	0.47	+	−4.4/−0.8	0/10
	250				0.66	−	−2.8/−0.8	0/10
VI	500	0.81	0.0/−1.0	2/5	0.54	+	−1.8/+0.2	3/10
	250				0.87	−	−0.6/+0.1	0/5
VII	500	1.13	0.0/+2.5	0/5	0.58	+	−2.4/−0.5	0/10
	250				0.80	−	−0.6/−0.1	0/5
VIII	500	0.87	−2.0/+0.5	0/5	0.48	+	−3.0/−0.5	0/10
	250				0.83	−	−2.1/−0.1	0/5
IX	500	0.96	+1.0/+1.5	0/5				
X	500	1.02	−2.5/+2.5	1/5	0.46	+	−1.8/+0.2	1/9
	250				1.04	−	−1.0/+0.1	0/5
XI	500	0.82	0.0/+3.5	2/5		Toxic		3/5
	250				0.97	−	−0.6/+0.2	0/10
XII	500	0.73	−4.0/+0.5	1/5				
XIII	500	0.95	+1.5/+1.5	1/5				
XIV	500	1.14	+2.0/+1.0	0/5				
XV	500	0.74	−2.0/+3.0	3/10	0.75	−	−4.5/+0.2	4/10
XVI	500	0.98	+1.0/+2.5	0/5	0.87	−	−0.8/+0.1	0/10
XVII	500	0.92	+1.5/+1.5	1/5				

[a] Compounds numbered same as in Table I. [b] Ratio of average diameters of tumors in treated (*T*) and untreated control (*C*) mice. [c] Average change in body weight of mice in grams, *T/C*. [d] Deaths of treated mice/number treated. [e] 500 mg./kg./day resulted in 100% mortality in S180 system.

on KBr pellets with a Beckman IR-5 spectrophotometer equipped with a NaCl prism.

Starting Materials.—The acetyl, dichloroacetyl, and benzoyl derivatives of amino acids were synthesized either according to published procedures or modifications of these procedures,[8] and in some instances were purchased from commercial sources. N-Dichloroacetyl-O-methyl-DL-serine was synthesized by the Schotten–Baumann procedure from O-methylserine. The latter was prepared from methyl acrylate according to the procedure given by Carter and West.[9] However, instead of treating the intermediate bromomethoxypropionic acid with concentrated NH_4OH in a glass-lined autoclave at 90–100° for 10–15 hr. to obtain the O-methylserine, we found it was possible to carry out this reaction at room temperature with 28% aqueous NH_3.

The nor-nitrogen mustards, bis(2-chloroethyl)amine and bis(2-chloropropyl)amine, were regenerated from their respective hydrochlorides[10] just before each synthesis.

N-Dichloroacetyl-DL-O-methylserine.—DL-O-Methylserine[9,11] (15.0 g., 0.125 mole) in 2 *N* NaOH solution (62.9 ml.) was cooled to −5°. Dichloroacetyl chloride (23.2 g., 0.15 mole) and 2 *N* NaOH solution (94.3 ml.), were added dropwise and simultaneously to maintain basic conditions and a temperature of about 0°. Stirring was then continued for 40 min., and the solution was filtered and treated with 25.7 ml. of concentrated HCl. The solution was evaporated to a mixture of oil and crystals. Several crystallizations from a mixture of ethyl acetate and petroleum ether (30–60°) yielded 7.75 g. (26.7%) of white crystals, m.p. 133–134°.

Anal. Calcd. for $C_6H_9Cl_2NO_4$: C, 31.32; H, 3.94; N, 6.09 Found: C, 31.07; H, 3.83; N, 6.05.

A. N,N-Bis(2-chloroethyl)-2-(dichloroacetamido)acetamid), (II).—N-Dichloroacetylglycine (9.7 g., 0.051 mole, m.p. 126–127°e. prepared according to the method of Abderhalden and coworkers,[8b] was added to a solution of bis(2-chloroethyl)amine (7.4 g., 0.051 mole) in 60 ml. of tetrahydrofuran. N,N′-Dicyclohexylcarbodiimide (10.76 g., 0.051 mole) dissolved in 60 ml. of tetrahydrofuran was added dropwise to the stirred solution during 30 min. Stirring was continued for an additional 30 min. and the practically quantitative precipitate of N,N′-dicyclohexylurea was removed by filtration and washed with tetrahydrofuran. The combined filtrate and washings were evaporated to dryness, and the residual solid mass was crystallized from a mixture of ethyl acetate and petroleum ether; yield 3.0 g. (18.6%), m.p. 62.5–63.5°. In other preparations yields up to 38.5% were obtained. The compound is soluble in warm ether or ethyl acetate and insoluble in benzene or petroleum ether. Its infrared absorption spectrum exhibited a maximum at 1631 cm.$^{-1}$ characteristic of a disubstituted amide linkage.

Anal. Calcd. for $C_8H_{12}Cl_4N_2O_2$: C, 30.99; H, 3.90; N, 9.04. Found: C, 30.87; H, 4.06; N, 9.10.

B. N,N-Bis(2-chloroethyl)-2-acetamido-DL-hydrocinnamide (VII).—N,N′-Dicyclohexylcarbodiimide (13.45 g., 0.065 mole) dissolved in 50 ml. of tetrahydrofuran was added dropwise over a period of 30 min. to a stirred solution of N-acetyl-DL-phenylalanine (13.5 g., 0.065 mole) and di(2-chloroethyl)amine (9.25 g., 0.065 mole) in 100 ml. of tetrahydrofuran. The reaction mixture was maintained at room temperature by a water bath. Stirring was continued for an additional hour, and the precipitated dicyclohexylurea (13.9 g., calcd. 14.6 g.) was removed by filtration and washed with tetrahydrofuran. The combined filtrate and washings were evaporated to yield a light yellow oil which was redissolved in ethyl acetate (100 ml.) and refrigerated for 1 hr. A further small amount of dicyclohexylurea (0.2 g.) precipitated and was removed by filtration. The filtrate was washed successively with 10% acetic acid (15 ml.), 2% $NaHCO_3$ (two 15-ml. portions), and water (15 ml.), dried ($MgSO_4$), and concentrated to yield 5.3 g. (70%) of a light yellow oil which slowly solidified. Several crystallizations from a mixture of

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(11) N. Izumiya, *J. Chem. Soc. Japan*, **71**, 214 (1950); *Chem. Abstr.*, **45**, 7011*i* (1951).

ethyl acetate and ether yielded approximately 50% of white crystals of VII, m.p. 119–121°.

Anal. Calcd. for $C_{15}H_{20}Cl_2N_2O_2$: C, 54.39; H, 6.09; N, 8.45. Found: C, 54.15; H, 6.21; N, 8.33.

Recovery procedure A yielded the same quality and quantity of product. However, in some instances only the washed solutions yielded crystalline products.

Antitumor Tests.—Procedures for determination of antitumor effects are described elsewhere for the Crocker sarcoma 180[12] and other mouse tumors.[13] Treatment was begun in mice bearing S180, sarcoma T241, or Ehrlich ascites 24 hr. after implantation of tumor, and in mice with C1025 or Ridgway osteogenic sarcoma 5 days after implantation. Each animal received 0.5 ml. of preparation intraperitoneally once daily for 7 consecutive days. Control tumor-bearing animals were similarly treated with 0.5% carboxymethylcellulose in 0.85% aqueous NaCl. Effects, evaluated 1 week after initiation of treatment (24 hr. after the last injection), were based on relative diameters of the solid tumors or on relative volumes of ascitic fluid for the Ehrlich carcinoma. Each experimental group contained five mice. In those instances in which a compound was retested at the same dose, the results of individual trials did not differ significantly and were averaged. A ratio between the average diameter of tumors in treated groups and that in controls (T/C) of ≤ 0.75 for S180, ≤ 0.60 for C1025 and Ridgway osteogenic sarcoma, ≤ 0.50 for E0771, and ≤ 0.70 for T241 are considered to be valid indications of inhibition of the growth of the tumors. In the Ehrlich ascites system a $T/C \leq 0.40$ is considered acceptable. Mortalities among mice in treated groups may be attributed to toxicity of the compounds; no deaths occurred in tumor-bearing control groups during the period of observation.

For injection the compounds were suspended by grinding in 0.5% carboxymethylcellulose in 0.85% aqueous NaCl. Suspensions were prepared daily just prior to injection.

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Chloroalkyl-N-sulfinylamines[1]

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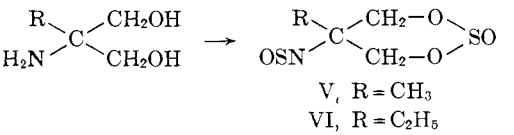
Chloroalkyl-N-sulfinylamines may be considered to be analogs of nitrogen mustards. In the course of studying the preparation of N-sulfinylamines we have prepared some of these chloroalkyl compounds for testing as antitumor agents (Table I). Their preparation can be readily accomplished by treating primary hydroxyalkylamines with thionyl chloride.

$$HO(CH_2)_nNH_2 + 2SOCl_2 \xrightarrow{\text{pyridine}} Cl(CH_2)_nNSO + \text{pyridine}\cdot HCl + SO_2$$

This method worked satisfactorily for the preparation of 2-chloro-N-sulfinylethylamine (I), 3-chloro-N-sulfinylpropylamine (II), 2-chloro-N-sulfinylpropylamine (III), and 2-chloro-1,1-dimethyl-N-sulfinylethylamine (IV). When 2-methyl- and 2-ethyl-2-amino-1,3-propanediol were treated with excess thionyl chloride, the amino groups were converted to sulfinylamino groups and the diols were converted to the cyclic sulfite ester.



V, R = CH_3
VI, R = C_2H_5

TABLE I

SCREENING DATA AGAINST WALKER 256 (SUBCUTANEOUS)[a]

Compd.	Dose, mg./kg.	Survivors	Animal wt. diff. ($T - C$)	Tumor wt. T/C	T/C, %
I	200	6/6	−20	5.8/5.4	107
	100	6/6	−10	6.4/5.4	118
	50	6/6	6	6.9/5.4	127
	25	6/6	4	5.3/5.4	98
II[b]	50	6/6		16.0/16.0	100
	10	6/6		15.5/16.0	97
III	200	6/6	0	7.3/5.4	135
	100	6/6	−1	6.2/5.4	114
	50	6/6	8	7.1/5.4	131
	25	6/6	9	5.9/5.4	109
IV	200	6/6	−11	6.0/5.4	111
	100	6/6	4	7.0/5.4	129
	50	6/6	−1	2.4/4.5	53
	25	6/6	−2	3.5/4.5	77
	12.5	6/6	−2	5.1/4.5	113
V	200	6/6	3	5.8/5.4	107
	100	6/6	6	6.5/5.4	120
	50	6/6	1	6.9/5.4	127
	25	6/6	3	5.7/5.4	105
VI	200	6/6	4	5.7/5.4	105
	100	6/6	3	5.8/5.4	107
	50	6/6	−2	3.3/4.5	73
	25	6/6	−5	4.1/4.5	91
	12.5	6/6	−5	3.8/4.5	84

[a] The biological testing was performed by the screening contractors of the Cancer Chemotherapy National Service Center. The authors are also indebted to the Sloan-Kettering Institute for preliminary screening of compound I. [b] These data are from tests with Dunning leukemia (solid).

Experimental

2-Chloro-N-sulfinylethylamine (I).—To a stirred, cooled solution of redistilled ethanolamine (61.1 g., 1.0 mole), pyridine (237 g., 3.0 moles), and chloroform (500 ml.) was added $SOCl_2$ (357 g., 3.0 moles) in $CHCl_3$ (250 ml.) over a period of 2 hr. The dark, viscous mixture was stored overnight in a refrigerator and then filtered to remove a small amount of insoluble material. The filtrate was divided into two equal parts and each part was extracted with three 200-ml. portions of Skellysolve A. The extracts were combined and evaporated under reduced pressure. The red oil thus obtained was distilled to give 27.4 g. (22%), b.p. 50–53° (6 mm.).

Anal. Calcd. for C_2H_4ClNOS: N, 11.15; S, 25.53. Found: N, 10.9; S, 25.1.

3-Chloro-N-sulfinylpropylamine (II).—Starting with 75.1 g. (1.0 mole) of 2-amino-1-propanol, the above procedure gave 84.2 g. (60%), b.p. 59–62° (4 mm.). Redistillation gave 67.1 g. (48%) of II, b.p. 61–63° (4 mm.).

Anal. Calcd. for C_3H_6ClNOS: N, 10.04; S, 22.97. Found: N, 9.67; S, 23.4.

2-Chloro-N-sulfinylpropylamine (III).—Starting with 75.1 g. (1.0 mole) of 1-amino-2-propanol, the above procedure gave 50 g. (36%) of III, b.p. 44–46° (2 mm.).

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