tion of adenosine at equimolar concentrations. The rate of deamination of 3'-deoxyadenosine was the same as that for adenosine.

Experimental Section

3'-Deoxy-2-fluoroadenosine.—A solution of 600 mg (2.26 mmoles) of 3'-deoxy-2-aminoadenosine (V)[5] in 6.8 ml of 48% aqueous HBF_4 at 0° was cooled to −10°, vigorously stirred, and 0.6 ml of a solution containing 300 mg of KNO_2 was added in 0.05-ml portions. The temperature was lowered to −30 to −40° and stirring was continued for 15 min. The pH of the reaction mixture was adjusted to 4 by adding 3.1 *N* KOH dropwise at −5 to −10°. The neutralization was continued to pH 6 at 0°. During the neutralization a total of 17 ml of BuOH-saturated water was added to facilitate stirring. After being stirred at 25° for 1 hr, the reaction solution was extracted with four 35-ml portions of BuOH-saturated water. The combined extracts were washed with four 15-ml portions of water-saturated BuOH. Concentration of the BuOH layer gave a residue (250 mg) which was purified by chromatography on 25 g of silica gel in Me_2CO–EtOH (99:1). Fractions containing only the desired product [R_f 0.5, tlc on silica in Me_2CO–EtOH (99:1)] were combined and concentrated. The residue (130 mg) was dissolved in 100 ml of EtOH, concentrated to 7 ml, and cooled. The crystalline 3'-deoxy-2-fluoroadenosine, mp 259–260°, so obtained amounted to 100 mg (17%). For analysis, a sample was washed (cold H_2O, EtOH, Et_2O) and dried at 50° for 4 hr at reduced pressure.

Anal. Calcd for $C_{10}H_{12}FN_5O_3$: C, 44.61; H, 4.49; N, 26.01; F, 7.06. Found: C, 44.93; H, 4.51; N, 26.08; F, 7.11.

3'-Deoxy-2-fluoroadenosine shows $[\alpha]D$ −65°, $[\alpha]_{578}$ −67° (*c* 0.165, ethanol); $\lambda_{max}^{H_2O}$ [mμ (ε × 10^{-3})] pH 1 262.5 (13.5), 267.5 (12.5); pH 7 262 (14.9), 268 (12.0); pH 13 261 (14.5), 267.5 (11.9).

In a larger preparation, starting with 5.1 g (19.2 mmoles) of V, the yield of IV was 900 mg (18%).

Action of Adenosine Deaminase on IV.—Individual solutions of IV and adenosine (8×10^{-4} *M*) in 3 ml of 0.05 *M* phosphate buffer (pH 7.5) were treated with equal amounts of calf intestine adenosine deaminase. The rate of deamination of the nucleosides was determined by the rate of the decrease in optical absorption at 265 mμ in a Cary spectrophotometer. At an enzyme concentration which brought about a change in optical density of 1.38 (equivalent to complete conversion to inosine) in 1 min with the adenosine sample, there was no measurable change in optical density with the solution containing 3'-deoxy-2-fluoroadenosine (IV) after 5 min. At this time the solution of IV was treated with an equimolar amount of adenosine. The latter was deaminated at the same rate (in 1 min) as was the adenosine in the absence of IV which indicated that IV is neither a substrate nor an inhibitor of the deaminase. In a separate experiment it was determined that 3'-deoxyadenosine was deaminated in about the same period of time as that required for adenosine.

Organic Disulfides and Related Substances. XXIV. Unsymmetrical *n*-Decylaminoethyl Disulfides as Antiradiation Drugs[1]

LAMAR FIELD, H. K. KIM, AND MICHAEL BELLAS

Department of Chemistry, Vanderbilt University, Nashville, Tennessee 37203

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We reported earlier that 2-(*n*-decylamino)ethyl 2-(*n*-decylamino)ethanethiolsulfonate dihydrochloride (**1**) was rated "good" as an antiradiation drug at a dose level of 50 mg/kg or less.[2] This result has prompted us to examine the *n*-decylaminoethyl system further by preparing two model unsymmetrical disulfides for evaluation (**2** and **3**). Disulfides **2** and **3** were prepared as shown by eq 1.

$$\underset{\mathbf{1}}{Cl^-(n\text{-}C_{10}H_{21}\overset{+}{N}H_2)(CH_2)_2SO_2S(CH_2)_2(\overset{+}{N}H_2\text{-}n\text{-}C_{10}H_{21})Cl^-} \xrightarrow{AcNH(CH_2)_nSH} Cl^-(n\text{-}C_{10}H_{21}\overset{+}{N}H_2)(CH_2)_2SS(CH_2)_nNHAc + \underset{\mathbf{3},\ n=3}{\underset{\mathbf{2},\ n=2}{}} + Cl^-n\text{-}C_{10}H_{21}\overset{+}{N}H_2)(CH_2)_2SO_2H \quad (1)$$

3-Acetamidopropanethiol, not previously readily available, was prepared by the reaction of 3-aminopropanethiol with acetyl chloride as described for 2-acetamidoethanethiol.[3] Usually in reactions like that shown in eq 1 we have isolated the unsymmetrical disulfide by making the reaction mixture basic, quickly extracting with organic solvent, and then acidifying the extract. This procedure unfortunately was impossible with the *n*-decylaminoethyl derivatives because of the formation of emulsions. However, good results were obtained by simply chromatographing the crude reaction mixture on acid-washed alumina.

The results from testing of **2** and **3** as antiradiation drugs are shown in Table I.[4] The marked difference between the radioprotective activities of the ethyl compound **2** and its propyl homolog **3** appears to be real, since both were checked. This strongly suggests that differences which might be thought trivial may be quite significant. Extensive differences of this kind have often been observed in other series of medicinal agents.

TABLE I

PROTECTIVE ACTIVITIES OF DISULFIDES **2** AND **3** IN MICE AGAINST IONIZING RADIATION[a]

Compd	Approx LD_{50}, mg/kg	Drug dose, mg/kg[b]	pH of prepn	Admind preirradiation, min	Survival (30 days), %	Act. rating
2	<50	<50	5.4	30	Insig	None to sl[c]
3	100	28	6	15	33	Good[c]
	100	56	6	15	67	

[a] 825 r (X-rays) or 1000 r (cobalt-60, γ rays). [b] Suspended in physiological saline solution containing 0.3% carboxymethylcellulose and 0.1% Tween 80. [c] On the basis of per cent survival: >45%, good; 25–44%, fair; 1–24%, slight; 0%, none.

It was also of interest to determine the resistance of **2** and **3** toward thermally induced disproportionation, as formulated in eq 2, since such values have been

$$2RSSR' \longrightarrow RSSR + R'SSR' \quad (2)$$

reported in earlier papers of this series for other classes of disulfides; possibly as such results continue to be obtained, correlations with antiradiation activity will emerge. Disulfide **2** disproportionated to the extent of 6% in 22 hr and of 22% in 72 hr (95% ethanol, 100°).

(1) (a) This investigation was supported by the U. S. Army Medical Research and Development Command, Department of the Army, under Research Contract No. DA-49-193-MD-2030. (b) Paper XXIII: L. Field and J. D. Buckman, *J. Org. Chem.*, in press.

(2) L. Field, A. Ferretti, R. R. Crenshaw, and T. C. Owen, *J. Med. Chem.*, **7**, 39 (1964).

(3) R. B. Martin, S. Lowey, E. L. Elson, and J. T. Edsall, *J. Am. Chem. Soc.*, **81**, 5089 (1959).

(4) Results were kindly provided by Drs. D. P. Jacobus, T. R. Sweeney, B. Alexander, and E. A. Steck of the Walter Reed Army Institute of Research. General procedures are described in ref 2. Both compounds, with the pH unadjusted, were administered intraperitoneally. The radiation was at a lethal level.

Despite the presence of the ammonium salt moiety, which usually decreases stability,[5] **2** seems considerably more stable than the salt 1,4-bis(2-aminoethyldithio)-butane dihydrochloride (19–35%, 3 hr) and indeed seems comparable to the amide of this butane compound (>20%, 72 hr) in being one of the most resistant to disproportionation we have encountered.[5] Similarly, disulfide **3** disproportionated to the extents of 6% in 22 hr and 13% in 72 hr.

Experimental Section[6]

2-Acetamidoethyl 2-(*n*-Decylamino)ethyl Disulfide Hydrochloride (2).—2-(*n*-Decylamino)ethyl 2-(*n*-decylamino)ethanethiolsulfonate dihydrochloride (1, 13.44 g, 25.0 mmoles)[7] was dissolved in a boiling mixture of CH_2Cl_2 and EtOH (500 ml, 1:1), and the solution was cooled to room temperature. 2-Acetamidoethanethiol (2.98 g, 25.0 mmoles)[8] then was added in one portion with stirring. The mixture was stirred for 3 hr more and then was chilled at *ca.* 10° overnight; filtration then removed traces of unreacted thiolsulfonate **1**. Evaporation of solvent below 30° gave solid, which was dissolved in a minimum of $CHCl_3$ (25 ml). The $CHCl_3$ solution was placed on a chromatographic column (24 × 300 mm of Merck acid-washed alumina)[9] and was eluted with $CHCl_3$. Evaporation of the first 500 ml of eluate gave crude **2** (6.51 g). Recrystallization from dioxane gave 5.00 g (54%) of pure **2**, mp 155–156°, unchanged by further recrystallization. The infrared spectrum showed the expected absorptions (cm^{-1}): 3420 (b), 3310 (s), 2440 (m) (characteristic of the *n*-decylamino hydrochloride moiety),[2] 1650 (s) and 1550 (s), in addition to a new absorption band at 1450 (s) not shown by either symmetrical disulfide, and nearly complete absences of 775 (m) and 760 (m) (doublet), which appeared in *n*-decylaminoethyl disulfide dihydrochloride. Similarly prepared material with a somewhat lower melting point (identical infrared spectrum) was analyzed. Thin layer chromatography (95% ethanol on Eastman Chromagram Type K301R; silica gel) showed only a single spot after development by exposure to iodine vapor (R_f 0.52).

Anal. Calcd for $C_{16}H_{33}ClN_2OS_2$: C, 51.79; H, 9.51; N, 7.55; S, 17.28. Found: C, 51.64; H, 9.65; N, 7.36; S, 17.17.

3-Acetamidopropanethiol.—In a modified procedure based on one for 3-amino-1-propanethiol of Turk and co-workers[10] and on an acetylation procedure essentially like one for 2-acetamidoethanethiol,[8] a solution of NaOH (40 g, 1.0 mole) in MeOH (200 ml) was thoroughly saturated with H_2S. A continuous stream of H_2S was maintained throughout the reaction. 3-Chloropropylamine hydrochloride (65 g, 0.50 mole)[11] dissolved in MeOH (70 ml) then was added during 0.5 hr with vigorous stirring at 50–60° (exothermic reaction). Solvent was then removed and $CHCl_3$ (350 ml) added, together with anhydrous $MgSO_4$ (30 g) to remove water. The mixture was heated under reflux for 15 min under N_2 and cooled, and solid then was removed by filtration. Acetyl chloride (25 ml, 0.35 mole) then was added dropwise to the rapidly stirred filtrate over *ca.* 20 min. After having been stirred for 3 hr more, the solution was shaken with saturated Na_2SO_4 solution (20 ml) and the $CHCl_3$ layer was separated and evaporated (760 mm) to 12.0 g (36%) of oil, which on titration with 0.1 *N* I_2–KI indicated 76% purity.

3-Acetamidopropyl 2-(*n*-Decylamino)ethyl Disulfide Hydrochloride (3).—3-Acetamidopropanethiol (5.50 g of 76% thiol, equivalent to 31.4 mmoles of pure thiol) was added to an EtOH–CH_2Cl_2 solution (500 ml, 1:1) of thiolsulfonate **1** (14.00 g, 26.0 mmoles), and the reaction mixture was worked up exactly as described for the 2-acetamidoethyl derivative (**2**). The crude product after being washed with acetone crystallized from EtOH–EtOAc as prisms (6.48 g, 65%), mp 122–123°, unchanged by further crystallization. Similarly prepared **3** (identical infrared spectrum) was analyzed.

Anal. Calcd for $C_{17}H_{37}ClN_2OS_2$: C, 53.02; H, 9.69; N, 7.28; S, 16.65. Found: C, 52.93; H, 9.40; N, 7.41; S, 16.85.

The infrared spectrum showed absorptions as expected and closely resembled the spectrum of **2**.

Disproportionation of 2-Acetamidoethyl and 3-Acetamidopropyl 2-(*n*-Decylamino)ethyl Disulfide Hydrochloride (2 and 3).—The disulfide **2** (about 1 mmole, precisely weighed) in EtOH (10 ml of 95%) was heated at 100° in a sealed vial wrapped with A. foil for either 22 or 72 hr, and the vial then was chilled in icel Solvent was removed from the contents of the vial, and the residue was rubbed well with purified dioxane (15 ml), in which only acetylcystamine, of components present, is significantly soluble. The resulting slurry was filtered, the residue was washed with a little more dioxane (9 ml), and the filtrate was evaporated. The acetylcystamine left then was dried to constant weight under reduced pressure; its identity and purity were established by its superimposable infrared spectrum. Calculations of the extent of disproportionation were done as usual.[12,13]

The propyl derivative **3** was done in the same way. Identity of the 3-acetamidopropyl disulfide was shown by melting point and mixture melting point and by comparison of the infrared spectrum with that of a sample prepared by reaction of H_2O_2 on 3-acetamidopropanethiol. With both **2** and **3** the reaction mixtures were homogeneous throughout at 100° and a precipitate only appeared on cooling.

(5) L. Field, A. Ferretti, and T. C. Owen, *J. Org. Chem.*, **29**, 2378 (1964).

(6) Melting points are corrected. Elemental analyses were by Galbraith Microanalytical Laboratories, Knoxville, Tenn. Infrared spectra were obtained using a Perkin-Elmer Model 137B or Beckman IR10 spectrophotometer with KBr pellets: s, signifies strong; m, medium; w, weak; b, broad. Evaporation of solvents usually was done under reduced pressure using a rotating evaporator.

(7) Kindly provided by Dr. Thomas R. Sweeney of the Walter Reed Army Institute of Research; prepared by the procedure of ref 2.

(8) R. Kuhn and G. Quadbeck, *Chem. Ber.*, **84**, 844 (1951).

(9) No difficulty was experienced with columns packed with $CHCl_3$. However, with a related series of decylaminoethyl disulfides, we occasionally got very poor separations, which we attribute to too basic an alumina. We got excellent results when such aluminas were stirred 30 sec in $CHCl_3$ saturated with HCl and then were packed in the column using this medium. Should separations with **2** or **3** give difficulty, therefore, this procedure may eliminate the difficulty.

(10) S. D. Turk, R. P. Louthan, R. L. Cobb, and C. R. Bresson, *J. Org. Chem.*, **27**, 2846 (1962).

(11) D. S. Tarbell and D. P. Cameron, *J. Am. Chem. Soc.*, **78**, 2731 (1956).

(12) Validity of this means of estimating disproportionation was established by making three sample mixtures of **2**, 2-(*n*-decylamino)ethyl disulfide dihydrochloride, and acetylcystamine, as though disproportionation of **2** had occurred to the extents of 10, 60, and 90%. Calculation of "disproportionation, %" for these mixtures from acetylcystamine, isolated as described, gave reasonable check results of 10, 61, and 85%. We are indebted to Dr. J. D. Buckman for suggesting the use of dioxane after a number of other separations had given poor results.

(13) L. Field, T. C. Owen, R. R. Crenshaw, and A. W. Bryan, *J. Am. Chem. Soc.*, **83**, 4414 (1961).

Trifluoromethyl Thiolsulfonates and Their Reactions with Mercaptans and Amines[1]

J. P. WEIDNER AND S. S. BLOCK

Department of Chemical Engineering, University of Florida, Gainesville, Florida

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Thiolsulfonates of the structure RSO_2S-aryl and RSO_2SCCl_3 (R = alkyl or aryl) have been prepared by the reaction of metal sulfinate and sulfenyl chloride. This paper, following our earlier brief reports, describes the synthesis by a similar procedure of the compounds RSO_2SCF_3 and unique reactions of these compounds with mercaptans and with amines.[2,3]

Trichloromethyl thiolsulfonates have been investi-

(1) This investigation was supported by U. S. Public Health Service Research Grant RH 00429, Division of Radiological Health.

(2) (a) S. S. Block, J. P. Weidner, and A. Walsh, Winter Meeting, American Chemical Society, Phoenix, Ariz., 1966, Abstract A56; (b) S. S. Block and J. P. Weidner, 153rd National Meeting of the American Chemical Society, Miami Beach, Fla., 1967, Abstract O 109.

(3) S. S. Block and J. P. Weidner, *Nature*, **214**, 478 (1967).