Synthesis of Nucleoside Analogs of 1,4-Oxathiane, 1,4-Dithiane, and 1,4-Dioxane (1)

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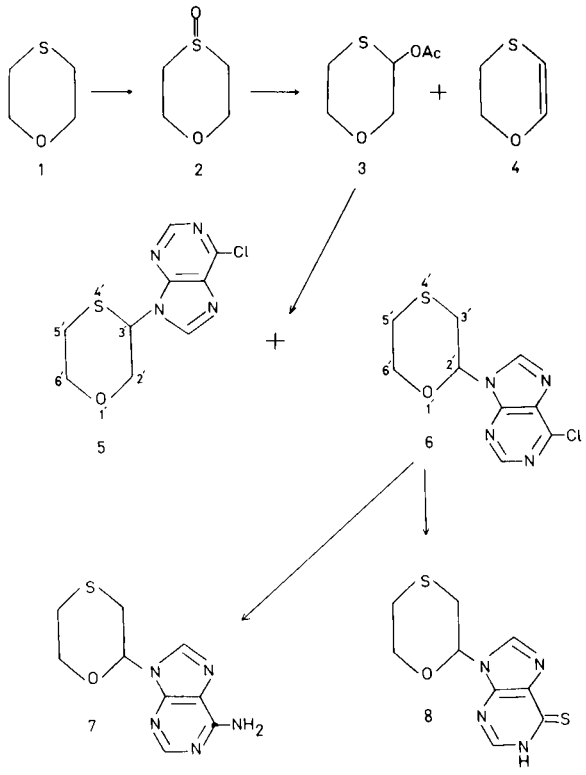
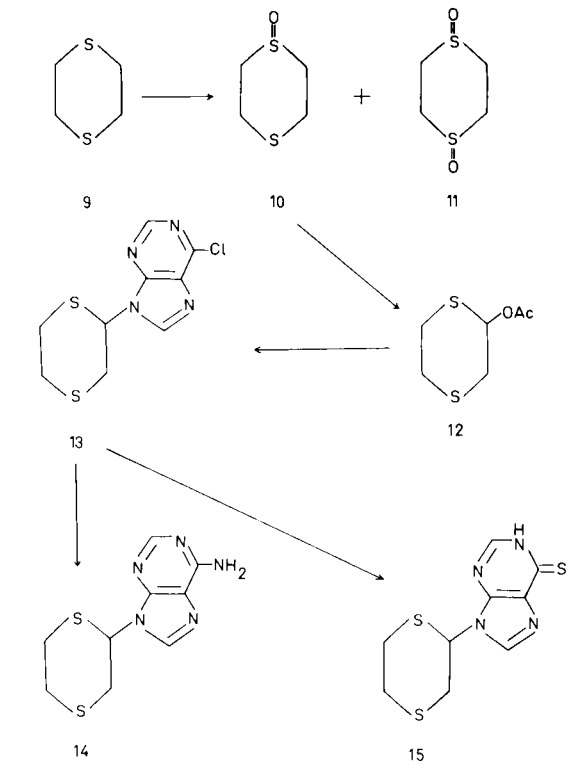
The two regioisomers 6-chloro-9-(1,4-oxathian-3-yl)-9*H*-purine (**5**) and 6-chloro-9-(1,4-oxathian-2-yl)-9*H*-purine (**6**) were obtained when 3-acetoxy-1,4-oxathiane (**3**) was subjected to the acid-catalyzed fusion procedure; compound **3** was prepared by a Pummerer reaction with 1,4-oxathiane 4-oxide (**2**). The nucleoside analog **6** could be converted into the adenine derivative **7** and 9-(1,4-oxathian-2-yl)-9*H*-purine-6(1*H*)thione (**8**). The following nucleoside analogs have also been synthesized: 6-chloro-9-(1,4-dithian-2-yl)-9*H*-purine (**13**), 9-(1,4-dithian-2-yl)adenine (**14**), 9-(1,4-dithian-2-yl)-9*H*-purine-6(1*H*)thione (**15**), and 6-chloro-9-(1,4-dioxan-2-yl)-9*H*-purine (**18**).

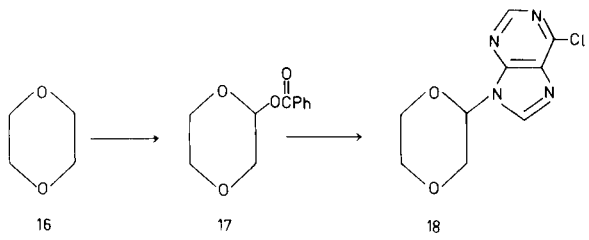
In a preliminary communication (1) from this laboratory, the synthesis of two nucleoside analogs of 1,4-oxathiane, namely, 6-chloro-9-(1,4-oxathian-3-yl)-9*H*-purine (**5**) and 6-chloro-9-(1,4-oxathian-2-yl)-9*H*-purine (**6**) was reported. Interestingly, the two regioisomers show different conformational preferences in chloroform-*d* solution, as determined from their nmr spectra (1,3). In the case of **5**, there is a preponderance of the conformer having the purine moiety in an axial orientation, whereas in the case of **6**, there is a preponderance of the equatorial form. A rationalization for this difference in terms of attractive or repulsive nonbonded interactions between lone pairs on the oxygen, sulfur, and the nitrogen atom at position 9 of the purine ring is under investigation. For this conformational study, the corresponding nucleoside analogs of 1,4-dithiane and 1,4-dioxane were also required. In the present article, full details of the synthesis of compounds **5** and **6**, and of 6-chloro-9-(1,4-dithian-2-yl)-9*H*-purine (**13**) and 6-chloro-9-(1,4-dioxan-2-yl)-9*H*-purine (**18**), are reported; the conversions of **6** into 9-(1,4-oxathian-2-yl)adenine (**7**) and 9-(1,4-oxathian-2-yl)-9*H*-purine-6(1*H*)thione (**8**), and of **13** into 9-(1,4-dithian-2-yl)adenine (**14**) and 9-(1,4-dithian-2-yl)-9*H*-purine-6(1*H*)thione (**15**), are also described. A further stimulus for the synthesis of all of these nucleoside analogs is the possibility of their being of biochemical or chemotherapeutic interest. It is known (4) that certain compounds obtained by condensation of periodate-oxidized nucleosides with isonicotinic acid hydrazide have antitumor activity and are useful for blocking the autoimmune processes in warm-blooded animals. These compounds have substituted morpholine structures; for example, periodate-oxidized adenosine affords *N*-[2-(9-adenyl)-3,5-dihydroxy-6-(hydroxymethyl)morpholino]isonicotinamide (5). It is known (6) also that many 9-(tetrahydropyran-2-yl)-9*H*-purines (7) exhibit significant antitumor activity. Interestingly, several organophosphorus derivatives of 1,4-oxathiane display (8) insecticidal and acaricidal activity.



Scheme 1



Scheme 2



Scheme 3

Foster and co-workers (9) have converted suitably protected glycopyranosides into derivatives of 2-hydroxy-1,4-oxathiane. In the present work, nucleoside-base derivatives of 1,4-oxathiane were synthesized from a non-carbohydrate precursor, namely, 1,4-oxathiane (**1**) itself, by way of a Pummerer reaction (10). McCormick and McElhinney (11) have previously employed the Pummerer reaction in a synthesis of carbohydrate derivatives in which the ring oxygen atom is replaced by sulfur.

1,4-Oxathiane (**1**) was converted into the hygroscopic sulfoxide **2** in 80% yield by oxidation with sodium metaperiodate by the method of Leonard and Johnson (12) (Scheme 1). Treatment of **2** with 1.5 equivalents of acetic anhydride in boiling benzene containing a trace of *p*-toluenesulfonic acid monohydrate for 3.5 hours afforded the chromatographically separable Pummerer-reaction product **3**, as a colorless liquid, and a small proportion of 1,4-oxathiene (**4**) (13,14). If the reaction mixture is heated for periods longer than 6 hours, then the formation of a third component is observed, which migrated in tlc at a slightly faster rate than 3-acetoxy-1,4-oxathiane (**3**), and the proportion of **3** is diminished. This third component is presumably 2-acetoxy-1,4-oxathiane, which could be formed by the addition of acetic acid to 1,4-oxathiene (**4**). An intimate mixture of compound **3** and 6-chloropurine was fused in the presence of *p*-toluenesulfonic acid monohydrate for 20 minutes. Fractionation of the complex mixture of products by preparative tlc on silica gel afforded the two major components, namely, 6-chloro-9-(1,4-oxathian-3-yl)-9*H*-purine (**5**) and 6-chloro-9-(1,4-oxathian-2-yl)-9*H*-purine (**6**), in approximately equal proportions (38% combined yield from **3**). The maximal uv absorption for each nucleoside analog at 264-266 nm in neutral, acid or basic solution is in agreement (15) with a 9-substituted purine. The structural differentiation of the regioisomers **5** and **6** was made initially on the basis of their proton magnetic resonance (pmr) spectra. It has been found (14, 16) that, in the spectrum of 1,4-oxathiane in carbon tetrachloride, the OCH_2 multiplet resonates at lower field (δ 3.88) than the SCH_2 multiplet (δ 2.57). Accordingly, the compound whose nmr spectrum showed a 4-proton multiplet at δ 5.0-3.7 and a 2-proton multiplet at δ 3.5-2.2, was assigned the 3-substituted 1,4-oxathiane structure (**5**), and the compound whose spectrum showed a 2-proton multiplet at δ 4.7-3.7 and a 4-proton multiplet at δ 3.5-2.1, was assigned the 2-substituted 1,4-oxathiane structure (**6**). If it is assumed that the 1,4-oxathiane rings of the nucleoside analogs **5** and **6** adopt chair conformations, then the value (~ 6 Hz) obtained for $J_{3',2'} + J_{3',2''}$ (17) from the nmr spectrum of **5** indicates a preponderance in chloroform-*d* of the conformer having the purine moiety in an axial orientation, whereas the value (11.5 Hz) obtained for $J_{2',3'} + J_{2',3''}$ for **6** indicates a preponderance of the equatorial form. The structures assigned to **5** and **6** have been corroborated in a recent study (3) by carbon-13 magnetic resonance (cmr) spectroscopy of these compounds and a related series of 1,4-oxathianes.

The isolation, from the condensation reaction, of compound **6**, in addition to the expected product **5**, is noteworthy. The formation of **6** is presumed to occur by the acid-catalyzed addition of 6-chloropurine to 1,4-oxathiene (**4**) (compare Refs. 7 and 13) produced during the condensation reaction. It is interesting that, if the crude mixture of 3-acetoxy-1,4-oxathiane (**3**) and 1,4-oxathiene (**4**) obtained from a Pummerer reaction with the sulfoxide **2** is subjected to an acid-catalyzed fusion with 6-chloropurine, then a very much greater proportion of nucleoside analog **6** is obtained than when the fusion is performed with pure 3-acetoxy-1,4-oxathiane (**3**). Treatment of **6** with methanolic ammonia gave crystalline 9-(1,4-oxathian-2-yl)ade-

nine (**7**) in 86.5% yield, whereas the use of methanolic potassium hydrosulfide afforded an essentially quantitative yield of crystalline 9-(1,4-oxathian-2-yl)-9*H*-purine-6(1*H*)-thione (**8**).

Oxidation of 1,4-dithiane (**9**) with 30% hydrogen peroxide in acetic acid by the literature method (18) leads to 1,4-dithiane 1-oxide (**10**) and the 1,4-dioxide **11** (Scheme 2). A Pummerer reaction with compound **10** afforded crystalline 2-acetoxy-1,4-dithiane (**12**). The acetate **12** was converted, in 42% yield, into 6-chloro-9-(1,4-dithian-2-yl)-9*H*-purine (**13**) by an acid-catalyzed fusion with 6-chloropurine. Compound **13** gave 9-(1,4-dithian-2-yl)adenine (**14**) in 94% yield, on treatment with methanolic ammonia, and 9-(1,4-dithian-2-yl)-9*H*-purine-6(1*H*)thione (**15**) in 89% yield, on treatment with methanolic potassium hydrosulfide.

2-Benzoyloxy-1,4-dioxane (**17**) was prepared by the reaction of *t*-butyl perbenzoate and 1,4-dioxane (**16**) in the presence of cuprous bromide as described by Sosnovsky and Yang (19) (Scheme 3). The benzoate **17** was converted, in 58% yield, into crystalline 6-chloro-9-(1,4-dioxan-2-yl)-9*H*-purine (**18**) by the acid-catalyzed fusion procedure.

Biological evaluation of all of the nucleoside analogs prepared in this work is in progress.

EXPERIMENTAL

Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. Infrared spectra were recorded with a Unicam SP 1000 spectrophotometer. Ultraviolet spectra were recorded with a Unicam SP 800B spectrophotometer. The pmr spectra were recorded at 60 MHz in chloroform-*d* with tetramethylsilane (δ 0.00) as internal standard, unless otherwise stated. Tlc was performed with Silica Gel G as the adsorbent; the developed plates were air-dried, sprayed with 5% ethanolic sulfuric acid, and heated at about 150°. The term "petroleum ether" refers to the fraction of b.p. 60-80°. 1,4-Oxathiane and 1,4-dithiane were purchased from Aldrich Chemical Company, Inc., Milwaukee, Wisconsin.

Pummerer Reaction with 1,4-Oxathiane 4-Oxide (**2**).

A solution of 1,4-oxathiane 4-oxide (12) (**2**, 4.5 g.) in benzene (50 ml.) containing acetic anhydride (5 ml.) and *p*-toluenesulfonic acid monohydrate (~ 10 mg.) was heated at reflux temperature for 3.5 hours. The solution was washed successively with aqueous sodium hydrogen carbonate (4 x 30 ml.) and water, and dried over magnesium sulfate. Evaporation of the solvent afforded an orange liquid, which was revealed by tlc [4:9 (v/v) ethyl acetate-petroleum ether] to consist of two components having Rf 0.78 and 0.52; the two components were isolated by chromatography on silica gel. The faster-moving component (15 mg.) was identified as 1,4-oxathiene (**4**), b.p. 58°/20 torr [lit. (13) b.p. 54°/20 torr]; the pmr-spectral data accorded with literature values (14). The slower-moving component (3 g.) was obtained as a colorless liquid, and was identified as 3-acetoxy-1,4-oxathiane (**3**); ir (film): 1739 (OAc) cm^{-1}; pmr: δ 5.4 (broad peak, 1H, H-3), 4.6-3.0 (6H, $-SCH_2-$, $-H_2COCH_2-$), 2.23 (s, 3H, OAc); cmr data for **3** are given in Ref. 3.

Acid-catalyzed Fusion of 3-Acetoxy-1,4-oxathiane (**3**) and 6-Chloropurine.

An intimate mixture of **3** (0.45 g.), 6-chloropurine (0.45 g.), and *p*-toluenesulfonic acid monohydrate (~10 mg.) was heated for 20 minutes on a steam bath; during this time the color of the reaction mixture changed from light yellow to dark brown. The syrupy mixture was extracted with hot ethyl acetate (3 x 10 ml.); evaporation of the extracts gave an orange syrup (0.43 g.), which was revealed by tlc [1:1 (v/v) ethyl acetate-benzene] to consist of several components with the two having Rf 0.40 and 0.52 being preponderant. The two major components were isolated by preparative tlc (using an 80 mg.-sample) as light yellow, amorphous solids. Recrystallization of the component having Rf 0.40 (25 mg.) from ether-petroleum ether afforded crystals of pure nucleoside analog **5**, m.p. 137-138° (20); uv λ max (ethanol): 265 nm (ϵ, 7,960) and 212 nm (ϵ, 11,639); λ max (0.1 *M* hydrochloric acid): 265 nm (ϵ, 7,960) and 210 nm (ϵ, 12,941); λ max (0.01 *M* sodium hydroxide): 266 nm (ϵ, 8,340) and 214 nm (ϵ, 10,809); ir (potassium bromide): 1587, 1563, and 1493 (puring ring) cm^{-1}; pmr: δ 8.83, 8.75 (1H-singlets, H-2,8), 5.57 (broad peak, 1H, $J_{3',2'} + J_{3',2''} \sim 6$ Hz, H-3'), 6.0-3.7 (4H, $-H_2COCH_2-$), 3.5-2.2 (2H, $-SCH_2-$).

Anal. Calcd. for $C_9H_9ClN_4OS$: C, 42.1; H, 3.5; Cl, 13.8; N, 21.8; S, 12.5. Found: C, 42.2; H, 3.6; Cl, 13.9; N, 21.6; S, 12.6.

Recrystallization of the component having Rf 0.52 (30 mg.) from chloroform-petroleum ether afforded crystals of pure nucleoside analog **6**, m.p. 108-109° (20); uv λ max (ethanol): 265 nm (ϵ, 9,710) and 210 nm (ϵ, 16,857); λ max (0.1 *M* hydrochloric acid): 264 nm (ϵ, 9,430) and 207 nm (ϵ, 15,143); λ max (0.01 *M* sodium hydroxide): 264 nm (ϵ, 9,430) and 212 nm (ϵ, 11,428); ir (potassium bromide): 1587, 1563, and 1493 (purine ring) cm^{-1}; pmr: δ 8.77, 8.37 (1H-singlets, H-2,8), 6.05 (dd, 1H, $J_{2',3'} + J_{2',3''} = 11.5$ Hz, H-2'), 4.7-3.7 (2H, $-OCH_2-$), 3.5-2.1 (4H, $-H_2CSCH_2-$).

Anal. Calcd. for $C_9H_9ClN_4OS$: C, 42.1; H, 3.5; N, 21.8; Cl, 13.8; S, 12.5. Found: C, 42.2; H, 3.6; N, 21.8; Cl, 13.8; S, 12.7.

Cmr data for nucleoside analogs **5** and **6** are given in Ref. 3.

In the separate experiment, the crude mixture (5.1 g.) of 3-acetoxy-1,4-oxathiane (**3**) and 1,4-oxathiene (**4**) obtained from a Pummerer reaction with the sulfoxide **2** was subjected to an acid-catalyzed fusion with 6-chloropurine as described above; column chromatography on silica gel of the reaction product afforded 0.1 g. of compound **5** and 2.8 g. of compound **6**.

9-(1,4-Oxathian-2-yl)adenine (**7**).

A solution of 6-chloro-9-(1,4-oxathian-2-yl)-9*H*-purine (**6**) (500 mg.) in 10% methanolic ammonia (50 ml.) was heated in a sealed pressure bottle at 90° for 3.5 hours. The solution was evaporated, and the residual, white powder was recrystallized from methanol to give compound **7** (400 mg., 86.5%), m.p. 178-183°; Rf 0.13 [tlc, 5:4:1 (v/v) ethyl acetate-benzene-methanol]; uv λ max (ethanol): 259 nm (ϵ, 12,222) and 212 nm (ϵ, 8,889); λ max (0.1 *M* hydrochloric acid): 256 nm (ϵ, 12,273) and 208 nm (ϵ, 10,909); λ max (0.01 *M* sodium hydroxide): 258 nm (ϵ, 13,273) and 214 nm (ϵ, 8,182); ir (potassium bromide): 3300 (NH), 1710 (NH_2), 1575 (purine ring) cm^{-1}; pmr (methyl sulfoxide-d_6): δ 8.13, 8.00 (1H-singlets, H-2,8), 7.10 (broad singlet, NH_2), 5.72 (dd, 1H, $J_{2',3'} + J_{2',3''} = 11.5$ Hz, H-2'), 4.6-2.2 ($-OCH_2-$ and $-H_2CSCH_2-$).

Anal. Calcd. for $C_9H_{11}N_5OS$: C, 45.6; H, 4.7; N, 29.5; S, 13.5. Found: C, 46.1; H, 4.6; N, 28.6; S, 13.6.

9-(1,4-Oxathian-2-yl)-9*H*-purine-6(1*H*)thione (**8**).

To a solution of 6-chloro-9-(1,4-oxathian-2-yl)-9*H*-purine (**6**) (330 mg.) in methanol (7 ml.) was added 2.5 ml. of methanolic potassium hydrosulfide [prepared by saturating a solution of potassium hydroxide (0.3 g.) in methanol (3 ml.) with hydrogen sulfide at 0°], and the reaction mixture was heated at reflux temperature for 15 minutes. The resultant precipitate was washed successively

with cold methanol and water. The powdery product **8** (320 mg., 98%) was soluble in methyl sulfoxide, but was practically insoluble in water, methanol, ethanol, chloroform, or diethyl ether; m.p. 245° dec.; uv λ max (ethanol): 324 nm (ε, 17,800) and 210 nm (ε, 10,160); λ max (ethanol containing a trace of hydrogen chloride): 324 nm (ε, 17,800) and 210 nm (ε, 10,160); λ max (ethanol containing a trace of sodium hydroxide): 315 nm (ε, 18,090), 235 nm (ε, 12,380), and 212 nm (ε, 14,920); ir (potassium bromide): 3500 and 1600 (NH) cm^{-1}; pmr (methyl sulfoxide-d_6): δ 13.4 (broad peak, NH), 8.26, 8.00 (1H-singlets, H-2,8), 5.70 (dd, 1H, $J_{2',3'}$ + $J_{2',3''}$ = 12.0 Hz, H-2'), 4.6-2.2 (-OCH_2O- and -H_2CSCH_2-). Compound **8** did not migrate in tlc in 4:1 or 3:2 (v/v) ethyl acetate-methanol.

Anal. Calcd. for $C_9H_{10}N_4OS_2$: C, 42.5; H, 4.0; N, 22.0; S, 25.2. Found: C, 42.6; H, 4.4; N, 21.7; S, 24.8.

2-Acetoxy-1,4-dithiane (**12**).

A solution of 1,4-dithiane 1-oxide (18) (**10**, 500 mg.) in benzene (5 ml.) containing acetic anhydride (1 ml.) and *p*-toluenesulfonic acid monohydrate (5 mg.) was heated at reflux temperature for 0.5 hour. The reaction mixture was diluted with benzene (50 ml.), and the solution was washed successively with aqueous sodium hydrogen carbonate and water, dried (magnesium sulfate), and evaporated. Chromatography of the residue (470 mg.) on silica gel, with benzene as eluent, afforded compound **12** (120 mg., 18.3%); elution with 5:4:1 (v/v) ethyl acetate-benzene-methanol gave 330 mg. of starting material (**10**). The chromatographically homogeneous sample of **12** was recrystallized from methanol; m.p. 85-86°; R_f 0.45 (tlc, benzene); ir (potassium bromide): 1745 (OAc) cm^{-1}; pmr: δ 6.2 (dd, 1H, H-2), 3.6-2.5 (6H, -SCH_2-), 2.17 (s, 3H, OAc).

Anal. Calcd. for $C_6H_{10}O_2S_2$: C, 40.4; H, 5.7; S, 36.0. Found: C, 40.5; H, 5.9; S, 35.7.

6-Chloro-9-(1,4-dithian-2-yl)-9*H*-purine (**13**).

An intimate mixture of 2-acetoxy-1,4-dithiane (**12**) (250 mg.), 6-chloropurine (200 mg.), and *p*-toluenesulfonic acid monohydrate (5 mg.) was heated at 70-80° on a water bath until it changed into a slurry (~5 minutes) and then *in vacuo* at this temperature for 15 minutes. The dry material was extracted with chloroform; the extract was filtered and the filtrate was evaporated to give a residue (30 mg.), which was revealed by tlc [1:4 (v/v) ethyl acetate-benzene] to consist of a trace of starting material (R_f 0.79), a major component having R_f 0.26, and a second new component which migrated close to the solvent front. The major component was isolated by chromatography on silica gel, with 1:19 (v/v) ethyl acetate-benzene as eluent, and was identified as nucleoside analog **13** (150 mg., 42%). Recrystallization from benzene gave **13** as needles, m.p. 155-157°; uv λ max (ethanol): 266 nm (ε, 11,605) and 212 nm (ε, 12,099); λ max [1:1 (v/v) ethanol-0.1 *M* hydrochloric acid]: 266 nm (ε, 11,605) and 212 nm (ε, 11,852); λ max [1:1 (v/v) ethanol-0.01 *M* sodium hydroxide]: 264 nm (ε, 10,617) and 216 nm (ε, 14,074); ir (potassium bromide): 1590, 1565, and 1480 (purine ring) cm^{-1}; pmr δ 8.77, 8.67 (1H-singlets, H-2,8), 5.90 (dd, 1H, $J_{2',3'}$ + $J_{2',3''}$ = 10.0 Hz, H-2'), 3.9-2.5 (6H, -SCH_2-).

Anal. Calcd. for $C_9H_9ClN_4S_2$: C, 39.6; H, 3.3; Cl, 13.0; N, 20.5; S, 23.5. Found: C, 39.8; H, 3.5; Cl, 12.9; N, 20.4; S, 23.8.

9-(1,4-Dithian-2-yl)adenine (**14**).

A solution of 6-chloro-9-(1,4-dithian-2-yl)-9*H*-purine (**13**) (250 mg.) in 10% methanolic ammonia (30 ml.) was heated in a sealed pressure bottle at ~100° for 3 hours. The reaction mixture was evaporated, and the residue was washed with hot benzene and recrystallized from methanol to give compound **14** (218 mg., 94%), m.p. 240-242°; R_f 0.40 [tlc, 2:3:1 (v/v) ethyl acetate-benzene-methanol]; uv λ (ethanol): 260 nm (ε, 15,470) and 212 nm (ε, 12,800); λ max (ethanol containing a trace of hydrogen chloride): 260 nm (ε, 15,200) and 215 nm (ε, 14,133); λ max (ethanol containing a trace of sodium hydroxide): 260 nm (ε, 15,470) and 215 (ε, 14,359); ir (potassium bromide): 3320 (NH), 1710 (NH_2), 1575 (purine ring) cm^{-1}; pmr (methyl sulfoxide-d_6): δ 8.22, 8.00 (1H-singlets, H-2,8), 7.12 (broad singlet, NH_2), 5.68 (dd, 1H, $J_{2',3'}$ + $J_{2',3''}$ = 11.5 Hz, H-2'), 3.9-2.3 (-SCH_2-).

Anal. Calcd. for $C_9H_{11}N_5S_2$: C, 42.7; H, 4.4. Found: C, 43.0; H, 4.7.

9-(1,4-Dithian-2-yl)-9*H*-purine-6(1*H*)thione (**15**).

To a suspension of 6-chloro-9-(1,4-dithian-2-yl)-9*H*-purine (**13**) (215 mg.) in methanol (4.5 ml.) was added 1.9 ml. of methanolic potassium hydrosulfide [prepared by saturating a solution of potassium hydroxide (0.3 g.) in methanol (3 ml.) with hydrogen sulfide at 0°], and the reaction mixture was heated at reflux temperature for ~15 minutes. The resultant precipitate was washed successively with methanol and water. The powdery product **15** (189 mg., 89%) was soluble in methyl sulfoxide, but was practically insoluble in water, methanol, or chloroform; m.p. 247° dec.; uv λ max (ethanol): 325 nm (ε, 13,034) and 218 nm (ε, 8,000); λ max (ethanol containing a trace of hydrogen chloride): 324 nm (ε, 12,360) and 217 nm (ε, 800); λ max (ethanol containing a trace of sodium hydroxide): 320 nm (ε, 12,359), 236 nm (ε, 7,191), and 212 nm (ε, 10,337); ir (potassium bromide): 3450 and 1600 (NH) cm^{-1}; pmr (methyl sulfoxide-d_6): δ 13.4 (broad peak, NH), 8.40, 8.01 (1H-singlets, H-2,8), 5.69 (dd, 1H, $J_{2',3'}$ + $J_{2',3''}$ = 11.5 Hz, H-2'), 3.9-2.3 (-SCH_2-). Compound **15** did not migrate in tlc in 4:1 or 3:2 (v/v) ethyl acetate-methanol.

Anal. Calcd. for $C_9H_{10}N_4S_3$: C, 40.0; H, 3.7; N, 20.7; S, 35.5. Found: C, 40.4; H, 4.2; N, 21.0; S, 34.8.

6-Chloro-9-(1,4-dioxan-2-yl)-9*H*-purine (**18**).

An intimate mixture of 2-benzoyloxy-1,4-dioxane (19) (**17**, 1.5 g.), 6-chloropurine (1 g.), and *p*-toluenesulfonic acid monohydrate (50 mg.) was heated at 70-80° on a water bath for 0.5 hour. The reaction mixture was extracted with chloroform (200 ml.), and the chloroform solution was washed successively with aqueous sodium hydrogen carbonate and water, dried (magnesium sulfate), and evaporated to give a residue (1.35 g.), which was revealed by tlc [1:1 (v/v) ethyl acetate-benzene] to consist predominantly of a new component having R_f 0.40. This component was isolated by chromatography on silica gel, with 2:3 (v/v) ethyl acetate-benzene as eluent, and was identified as nucleoside **18** (1.0 g., 58%). Recrystallization from *n*-hexane-benzene gave **18** as needles, m.p. 115-116°; uv λ max (ethanol): 263 nm (ε, 8,000) and 209 nm (ε, 8,000); λ (ethanol containing a trace of hydrogen chloride): 263 nm (ε, 8,000) and 209 nm (ε, 7,800); λ max (ethanol containing a trace of sodium hydroxide): 263 nm (ε, 7,800) and 213 nm (ε, 10,400); ir (potassium bromide): 1600, 1570, and 1500 (purine ring) cm^{-1}; pmr: δ 8.59, 8.32 (1H-singlets, H-2,8), 5.90 (dd, 1H, $J_{2',3'}$ + $J_{2',3''}$ = 8.5 Hz, H-2'), 4.2-3.7 (6H, -OCH_2-).

Anal. Calcd. for $C_9H_9ClN_4O_2$: C, 44.9; H, 3.8; N, 23.3. Found: C, 45.3; H, 4.1; N, 23.4.

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