TABLE I

λ_{max} OF PRODUCTS FROM FLAVYLIUM SALTS AT pH 9 AND pH 12

Flavylium compounds	pH 8–10: Product λ_{max} mμ (log ε)	pH 8–10: Product on acidification λ_{max} mμ (log ε)	pH 12: Product λ_{max} mμ (log ε)	pH 12: Product on acidification λ_{max} mμ (log ε)
4′-Hydroxy-3′,7-dimethoxy	480 (4.43)	413 (4.45)	444 (4.48)	374 (4.37)
4′-Hydroxy-7-methoxy	472 (4.43)	410 (4.45)	435 (4.38)	370 (4.26)
7-Hydroxy-7-Hydroxy-3′,4′-dimethoxy	483 (4.68)	411 (4.48)	481 (4.53)	371 (4.26)
7-Hydroxy-4′-methoxy-	483 (4.70)	414 (4.44)	483 (4.56)	371 (4.28)
	483 (4.71)	413 (4.47)	481 (4.58)	370 (4.28)

chalcone. The complete reaction sequence postulated for 4′-hydroxy-7-methoxyflavylium chloride is summarized in Chart I.

7-Keto anhydro bases behave similarly. Thus, 7-hydroxy-4′-methoxyflavylium chloride, adjusted to pH 12.2, rapidly forms the ionized *cis*-chalcone, λ_{max} 481 mμ, log ε 4.58, which, on acidification to pH < 1, gives the unionized *cis*-chalcone, λ_{max} 370 mμ, log ε 4.28 (Fig. 5). At pH 9.9, however, the flavylium salt forms a yellow compound, λ_{max} 483 mμ, log ε 4.71, which differs distinctly from the ionized *cis*-chalcone, since on acidification to pH < 1 it immediately gives a bright lemon yellow compound, λ_{max} 413 mμ, log ε 4.47. On standing in the acid solution, this yellow product (protonated *trans*-chalcone) slowly regenerates the original flavylium salt (λ_{max} 457 mμ, log ε 4.65). Similar structural changes have been observed with the other flavylium salts listed in Table I. In each case the products formed at pH 9–10 and pH 12 are clearly distinguished by acidification to yield either yellow, protonated *trans*-chalcones (λ_{max} 410–414 mμ) or un-

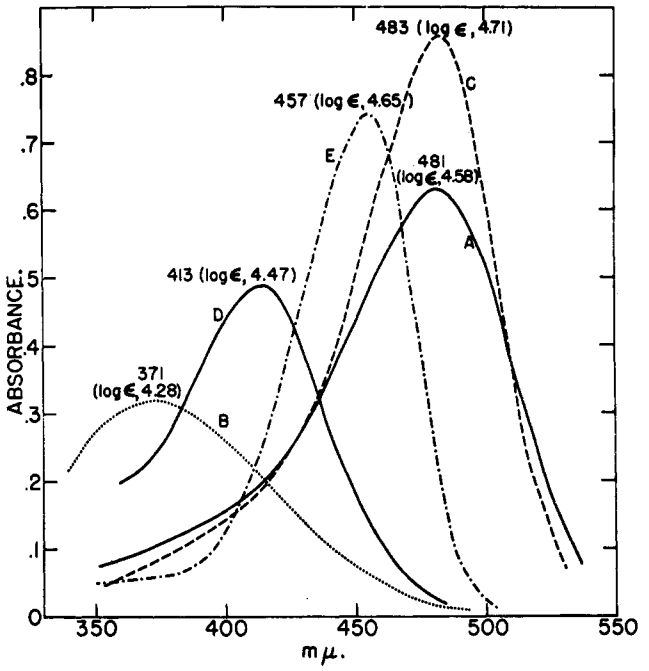

Fig. 5.—Spectrum of 7-hydroxy-4′-methoxyflavylium chloride (4.8×10^{-3} g./l.): (A) at pH 12.2; (B) acidification of A to pH < 1, spectrum taken at once; (C) at pH 10.0; (D) acidification of C to pH < 1, spectrum taken at once; (E) spectrum of B and D after standing 6 hr. and 71 hr., respectively.

ionized, almost colorless, *cis*-chalcones (λ_{max} 370–374 mμ).

Experimental

The flavylium salts used in this investigation are known compounds. They were prepared by Robinson's general methods, *vis.* acid condensation of the appropriate O hydroxyaldehydes and acetophenones in ethyl acetate or acetic acid solutions as described in Part I.[5]

The spectra of the flavylium salts used in this investigation were determined in buffered solutions[5] in 1-cm. silica cells.

The Synthesis of 5′-Deoxy-5′-S-(3-methylthiopropylamine)sulfoniumadenosine ("Decarboxylated S-Adenosylmethionine")

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5′-Deoxy-5′-S-(3-methylthiopropylamine)sulfoniumadenosine, the biological precursor of spermidine, has been synthesized by the condensation of 2′,3′-isopropylidene-5′-toluene-*p*-sulfonyladenosine and 3-thiopropylamine followed by removal of the acetonide group and subsequent methylation of the thioether. The corresponding (2-methylthioethylamine)- and (4-methylthiobutylamine)sulfoniumadenosine derivatives have been prepared in a similar way.

Although the specific biological function of the naturally occurring polyamines spermidine (1) and spermine (2) is not known, they have been shown to be

$NH_2(CH_2)_3NH(CH_2)_4NH_2$ (1) $\quad NH_2(CH_2)_3NH(CH_2)_4NH(CH_2)_3NH_2$ (2)

effective as growth factors for certain organisms and to exert a stabilizing effect on mitochondria and on DNA.[2-4] The path of biosynthesis of these compounds has been clarified by studies using labeled methionine and putrescine (1,4-diaminobutane) and the following scheme has been proposed on the basis of the labeling patterns in the various enzymatic products.[5]

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(2) For a full review on spermidine and spermine, see H. Tabor, C. W. Tabor, and S. M. Rosenthal, *Ann. Rev. Biochem.*, **30**, 579 (1961).

(3) H. Tabor, *Biochem. Biophys. Res. Commun.*, **4**, 228 (1961).

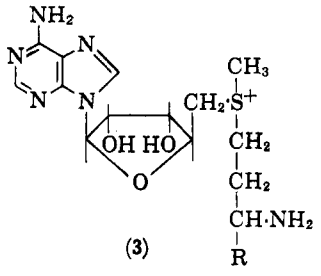
(4) H. Tabor, *Biochemistry*, **1**, 496 (1962).

(5) H. Tabor, S. M. Rosenthal, and C. W. Tabor, *J. Biol. Chem.*, **233**, 907 (1958).

ATP + L-methionine ⟶
S-adenosyl-L-methionine[6] (**3**, R = COOH)

"S-adenosyl-L-methionine ⟶
"Decarboxylated S-adenosylmethionine"[7] (**3**, R = H) + CO_2

"Decarboxylated S-adenosylmethionine" + putrescine ⟶
5'-methylthioadenosine + spermidine



(3)

The sulfonium derivative, S-adenosylmethionine, is known to be the principal intermediate in the activation of methionine for transmethylation,[8] but its decarboxylated homolog 5'-deoxy-5'-S-(3-methylthiopropylamine)sulfoniumadenosine[7] has not hitherto been found in nature. It was, therefore, considered desirable to synthesize the compound itself and certain of its homologs in order to establish their structure and to provide adequate amounts of material for further enzymatic work, including studies on structural specificity.[9]

The most satisfactory route to sulfonium nucleosides of adenosine has been found to be the prior synthesis of the corresponding thioether and its subsequent methylation with methyl iodide.[10] The thioether itself may be prepared by the condensation in liquid ammonia of the appropriate sodiomercaptide with 2',3'-isopropylidene-5'-toluene-*p*-sulfonyladenosine[10,11] followed by the removal of the acetonide group by mild acid hydrolysis. This general method has been followed in these preparations of the 5'-deoxy-5'-S-(*n*-thioalkylamine)adenosine precursors of the sulfonium nucleosides.

The intermediate aminothiols were used as their S-benzyl derivatives except in the case of 2-thioethylamine.[12] 3-Benzylthiopropylamine itself was obtained by the lithium aluminum hydride reduction[13] of 3-benzylthiopropionitrile.[14] 4-Benzylthiobutylamine was prepared from 4-bromobutylphthalimide or alternatively the bromo compound was converted to the disulfide and treated with hydrazine hydrate to yield the corresponding di(aminobutyl) disulfide. The unsubstituted 4-thiobutylamine hydrochloride also was synthesized after considerable modification of the published method[15] (see Experimental).

When condensed with 2',3'-isopropylidene-5'-toluene-*p*-sulfonyladenosine and worked up in the usual way the various thioalkylamine derivatives afforded the isopropylidene derivatives of the desired thioethers. After removal of the isopropylidene group methylation was readily carried out with methyl iodide in a mixture of formic and acetic acids and the reaction could be followed by the appearance of material which moved rapidly towards the cathode on paper electrophoresis.

The separation of S-adenosylmethionine from S-adenosylhomocysteine has been considerably facilitated by the precipitation of the sulfonium compound as its Reineckate salt.[16] In the present series both the thioether and the sulfonium derivative yield Reineckates under slightly acid conditions. Similarly, it was not possible to effect a useful chromatographic separation using ion exchange resins at the acid pH values necessary to avoid the rapid decomposition known to occur under alkaline conditions with sulfonium nucleosides.[17,18] However, the sulfonium derivatives were readily separated from the unchanged thioethers by precipitation as their flavianates. The flavianates were suspended subsequently in dilute acid and extracted repeatedly with 2-butanone or alternatively, the precipitates were dissolved in a large volume of water and passed slowly down a column of Dowex 1 cation-exchange resin in the acetate form. While the latter method avoids the successive extractions it suffers from the disadvantage that relatively large volumes of aqueous solution must be used.

The three sulfonium compounds were indistinguishable on paper electrophoresis at pH 5.8 and on paper chromatography in a number of solvent systems. No differences could be detected in their rates of decomposition under alkaline conditions.

Experimental

3-Benzylthiopropylamine (ref. 13).—A solution of 3-benzylthiopropionitrile[11] (25.0 g.) in dry ether (150 ml.) was added over a period of about 1 hr. to a vigorously stirred suspension of lithium aluminum hydride (7.3 g.) in dry ether (200 ml.). A stream of helium was passed slowly through the flask during the addition and ice cooling was applied sufficient to maintain a gentle reflux. After the addition of the nitrile the reaction mixture was heated under reflux for 1 hr. and finally cooled in ice. Ethyl acetate (200 ml.) was added cautiously, followed by water (100 ml.). The mixture was filtered and the precipitate washed with a little acetone and then washed extensively with ether. The filtrate was extracted with ether and the combined ethereal extracts dried over anhydrous sodium sulfate. Ether was removed under reduced pressure and the residual oil distilled through a Claisen head. 3-Benzylthiopropylamine (15.3 g., 60%) was obtained as a white, mobile, virtually odorless oil, b.p. 124° (3 mm.).

(6) Subsequent work on the stereochemistry of this compound [G. de la Haba, G. A. Jamieson, S. H. Mudd, and H. H. Richards, *J. Am. Chem. Soc.*, **81**, 3975 (1959)] has shown that the partial specific rotation of the sulfonium center in the nucleoside is *levo* and that it may be described as (−)-S-adenosyl-L-methionine. Since Tabor, *et al*, ref. 5, have shown that the nucleoside isolated from liver or from yeast is fully active in the bacterial system it is probable that both the sulfonium nucleosides involved in this system are also of the *levo* configuration.

(7) Although the terms S-adenosylhomocysteine, S-adenosylmethionine ("active methionine"), and "decarboxylated S-adenosylmethionine" suggest the biological origin of these compounds, they do not emphasize the sulfonium nature of the last two and are otherwise unacceptable from the point of view of nomenclature. Since these compounds may be considered as nucleosides, since they derive biologically from ATP, and since certain of their properties are dependent upon their dual function as adenosine derivative and sulfonium compounds, they may be described as derivatives of 5'-deoxy-5'-sulfoniumadenosine. In this communication "decarboxylated S-adenosylmethionine" will be termed 5'-deoxy-5'-S-(3-methylthiopropylamine)sulfoniumadenosine.

(8) G. L. Cantoni, *J. Biol. Chem.*, **204**, 403 (1953).

(9) Enzymatic studies will be reported elsewhere. However, preliminary results indicate that the synthetic compound is active in the partially purified *E. coli system* (C. W. Tabor, personal communication).

(10) J. Baddiley and G. A. Jamieson, *J. Chem. Soc.*, 1085 (1955).

(11) W. Sakami, "Biochemical Preparations," Vol. 8, A. Meister, Ed., John Wiley and Son, Inc., New York, N. Y., 1961, pp. 5 and 8.

(12) Obtained from Mann Research Laboratories, Inc., New York, N. Y.

(13) A. Kjaer, F. Marcus, and J. Conti, *Acta Chem. Scand.*, **7**, 1370 (1953).

(14) C. D. Hurd and L. H. Gershbein, *J. Am. Chem. Soc.*, **69**, 2328 (1947).

(15) T. Wieland and H. Hornig, *Ann. Chem.*, **600**, 12 (1956).

(16) G. de la Haba and G. L. Cantoni, *J. Biol. Chem.*, **234**, 603 (1959).

(17) L. W. Parks and F. Schlenk, *ibid.*, **230**, 295 (1958).

(18) W. Frank, J. Wieczorkowski, N. A. Hughes, and J. Baddiley, *Proc. Chem. Soc.*, 449 (1961).

Anal. Calcd. for $C_{10}H_{15}NS$: C, 66.24; H, 8.28; N, 7.73. Found: C, 65.02; H, 8.16; N, 7.20.

A portion of the oil was dissolved in dry ether and gaseous hydrogen chloride passed through the solution to yield white crystals of 3-benzylthiopropylamine hydrochloride, m.p. 68–72°,[19] after two recrystallizations from alcohol–ether, m.p. 76°.

Anal. Calcd. for $C_{10}H_{16}ClNS$: C, 55.2; H, 7.37; N, 6.45. Found: C, 55.21; H, 7.45; N, 6.22.

4-Bromobutylphthalimide.—This compound was prepared by applying the modification of Sheehan and Bolhoffer[20] to the original synthesis of Rumpf.[21] It was obtained as white glistening plates (60%, m.p. 78–79°; lit.[21] m.p. 79°).

4-Benzylthiobutylphthalimide.—ω-Toluenethiol (10.4 g.) was added to a solution of metallic sodium (1.92 g.) in absolute ethanol (50 ml.). A solution of 4-bromobutylphthalimide (23.5 g.) in dimethylformamide (100 ml.) was then added. The resulting mixture was warmed on the steam bath for 30 min. and then cooled to room temperature and diluted with a large volume of water (*ca.* 2 l.). The precipitated oil, which crystallized on standing overnight in the refrigerator, was removed by filtration and recrystallized from ethanol or cyclohexane yielding 21 g. (78%), m.p. 64°.

Anal. Calcd. for $C_{19}H_{19}NO_2S$: C, 70.2; H, 5.84. Found: C, 69.97; H, 5.98.

4-Benzylthiobutylamine Hydrochloride.—4-Benzylthiobutylphthalimide (9.0 g.) in methanol (50 ml.) was treated with 95% hydrazine hydrate (4.5 ml.) on the steam bath for 1.5 hr. during which time a curdlike precipitate formed. Methanol was removed under reduced pressure and the residue was shaken mechanically for 1 hr. with a mixture of 4 *N* ammonia (100 ml.) and chloroform (100 ml.).[22] The organic layer was separated and the aqueous layer re-extracted with chloroform (50 ml.). The combined organic layers were extracted with four 50-ml. portions of 3 *N* acetic acid. The acid extracts were then rendered basic with ammonia (*d* 0.880) and extracted with ether. The ethereal extracts were dried (sodium sulfate) and anhydrous hydrogen chloride passed through the solution. The precipitate (5.1 g, m.p. 128°, from aqueous acetone) was collected and washed with a little ether.

Anal. Calcd. for $C_{11}H_{10}NS\cdot HCl$: C, 57.00; H, 7.83; N, 6.04; Cl, 15.30. Found: C, 57.09; H, 7.85; N, 5.96; Cl, 14.78.

Dithiobutylamine Dihydrochloride.—A solution of metallic sodium (1.8 g.) in absolute ethanol (50 ml.) was saturated with hydrogen sulfide and to the mixture was added a solution of 4-bromobutylphthalimide (14.1 g.) in dimethylformamide (50 ml.). After being heated on the steam bath for 1 hr. the flask was cooled to room temperature and the contents diluted with water (*ca.* 300 ml.). The precipitated oil crystallized after about 1 hr. and was recrystallized once from ethanol. The product (11.3 g.) was converted to the disulfide without further purification. The crude phthalimidobutanethiol (11.1 g.) was dissolved in absolute ethanol (100 ml.) and to this was added a solution of iodine (6.0 g.) in ethanol followed by alcoholic potassium hydroxide sufficient to bring the solution to near neutrality.[23] The pale yellow solution was then warmed on the steam bath for 15 min.; hydrazine hydrate (95%, 7.5 ml.) was then added and heating continued for 1 hr. Solvent was removed at the pump and the residue worked up by the method of Barber and Wragg[22] as used for 4-benzylthiobutylamine. Dithiobutylamine dihydrochloride (5.9 g., 78%) was recrystallized from hot ethanol; m.p. 259° dec.

Anal. Calcd. for $C_8H_{20}N_2S_2\cdot 2HCl$: C, 34.15; H, 7.88; Cl, 25.2. Found: C, 34.40; H, 8.00; Cl, 25.40.

Phthalimidobutyl Exthylxanthate.—This compound was prepared according to the method of Wieland and Hornig[15] in a yield of 82%. It had m.p. 60° (lit. m.p. 78°) and analyzed well for the xanthate ester.

Anal. Calcd. for $C_{15}H_{17}NOS_2$: C, 55.72; H, 5.30; N, 4.33. Found: C, 55.98; H, 5.34; N, 4.48.

4-Thiobutylamine Hydrochloride.—Phthalimidobutyl ethylxanthate (15.0 g.) was refluxed overnight in a mixture of concentrated hydrochloric acid (250 ml.) and glacial acetic acid (250 ml.). Next morning the solution was evaporated to dryness under reduced pressure and water added to the crystalline residue. Insoluble material was removed by filtration and washed with a little water. The filtrate and washings were combined and evaporated to give a sirupy residue. A small portion of this residue was warmed with acetone and the crystalline product removed by filtration. Di(4-thiobutylamine hydrochloride) dimethylmercaptal was obtained as white prisms, m.p. 172°, after several recrystallizations from ethanol–acetone.

Anal. Calcd. for $C_{11}H_{28}Cl_2N_2S_2$: C, 40.86; H, 8.73; Cl, 21.94. Found: C, 40.67; H, 8.70; Cl, 22.10.

The sirupy residue was dissolved in the minimum volume of water and applied to a column (3 × 75 cm.) of Dowex 50 (X8, 100–200 mesh) cation-exchange resin in the hydrogen form. A linear gradient of 4 *N* hydrochloric acid (2 l.) against water (2 l.) was applied to the column and 25-ml. fractions were collected. Nitroprusside reacting material appeared in fractions 120–165. These were assayed quantitatively with N-ethylmaleimide,[24] and the tubes containing the highest concentration of thiol (125–155) were combined and evaporated to dryness. The product was taken up in alcohol, precipitated by the addition of ether and filtered. The product (4.1 g., 67%) was obtained as a white, extremely hygroscopic powder which was homogeneous to the ninhydrin and nitroprusside sprays after chromatography in the following solvents.

		R_f
(a)	1-Butanol–acetic acid–water (4:1:5)	0.40
(b)	1-Butanol saturated with 1 *N* HCl	.30
(c)	Ethanol–water (8:2)	.57
(d)	*sec.*-Butanol–formic acid–water (75:15:10)	.14

However, a small amount of the product was insoluble in concentrated hydrochloric acid. This was removed by filtration through a sintered glass funnel and the filtrate was evaporated to dryness and the residue recrystallized several times from butanol–ether; m.p. 122–124°.

Anal. Calcd. for $C_{14}H_{11}NS\cdot HCl$: C, 33.90; H, 8.54; N, 9.89. Found: C, 33.83; H, 8.30; N, 9.81.

2′,3′-Isopropylidene-5′-deoxy-5′-S-(3-thiopropylamine)adenosine.—A two-necked 1-l. flask was provided with a stirrer and the other opening was closed by a sodium hydroxide tube to prevent the ingress of moisture. Dry ammonia (*ca.* 300 ml.) was condensed into the flask and 3-benzylthiopropylamine (3.2 g.) was carefully added. The mixture was stirred and metallic sodium was added in small pieces until a blue color was obtained which was permanent for 5–10 min. 2′,3′-Isopropylidene-5′-toluene-*p*-sulfonyladenosine (9.2 g.) was then added carefully to the liquid ammonia solution. Stirring was discontinued after about 10 min. and liquid ammonia was allowed to evaporate over a period of several hours, the final traces being removed under reduced pressure at the water pump.

The solid residue was then shaken with equal volumes of chloroform (100 ml.) and cold dilute 1 *N* sulfuric acid (100 ml.). The acid layer was separated and the organic layer re-extracted with a further portion of dilute sulfuric acid. The combined acid extracts were then made basic and the precipitated oil extracted with three 50-ml. portions of chloroform. The chloroform layer was washed once with water (*ca.* 50 ml.) and dried over anhydrous sodium sulfate. Chloroform was removed from the combined organic extracts under reduced pressure and the residual oil taken up in hot water, treated with a little decolorizing charcoal, filtered and cooled. 2′,3′-Isopropylidene-5′-deoxy-5′-S-(3-thiopropylamine)adenosine sesquihydrate (4.1 g., 53%) was obtained as glistening plates, m.p. 66–68°.

Anal. Calcd. for $C_{16}H_{24}N_6O_3S\cdot 1.5\ H_2O$: C, 50.62; H, 6.36; N, 22.09; wt. loss on drying, 6.63. Found: C, 50.39; H, 6.49; N, 22.04; wt. loss (100° under high vacuum for 3 hr.), 6.01.

5′-Deoxy-5′-S-(3-thiopropylamine) Adenosine Bisulfate.—The isopropylidene nucleoside (3.0 g.) was dissolved in 1 *N* sulfuric acid (40 ml.) and left at room temperature for 48 hr. Ethanol was then added to the solution to produce a slight turbidity and the flask chilled in ice. Crystalline material (2.2 g.) was filtered off and washed with a little 50% aqueous ethanol and with absolute ethanol. Additional crystalline material (0.5 g.) was obtained by the addition of a large excess of alcohol to the mother

(19) Analyses were performed by the Microanalytical Laboratory of this institute under the direction of Mr. Harold G. McCann. All melting points are uncorrected.

(20) J. C. Sheehan and W. A. Bolhoffer, *J. Am. Chem. Soc.*, **72**, 2786 (1950).

(21) P. Rumpf, *Bull. soc. chim. France*, **5**, 871 (1938).

(22) H. J. Barber and W. R. Wragg, *J. Chem. Soc.*, 1331 (1947).

(23) L. A. Subluskey and L. C. King, *J. Am. Chem. Soc.*, **73**, 2647 (1951).

(24) J. D. Gregory, *ibid.*, **77**, 3922 (1955).

liquors. Both crops melted at 173–175° raised to 180–183° dec., after recrystallization from aqueous alcohol.

Anal. Calcd. for $C_{13}H_{21}N_6O_3S \cdot HSO_4$: C, 35.55; H, 5.28; N, 19.14; SO_4, 21.87. Found (on material dried 7 hr. at 100° *in vacuo*): C, 35.70; H, 5.31; N, 19.13; SO_4, 21.55.

2′,3′-Isopropylidene-5′-deoxy-5′-S-(4-thiobutylamine)adenosine.—This compound was prepared in the usual way by treating dithiobutylamine dihydrochloride (1.25 g.) with sodium in liquid ammonia to a permanent blue color and then condensing the resulting mercaptide with 2′,3′-isopropylidene-5′-toluene-*p*-sulfonyladenosine (4.6 g.). 2′,3′-Isopropylidene-5′-deoxy-5′-S-(4-thiobutylamine)adenosine sesquihydrate (2.45 g.) had m.p. 59° (from hot water).

Anal. Calcd. for $C_{17}H_{26}N_6O_3S \cdot 1.5\ H_2O$: C, 48.43; H, 6.93; N, 19.93. Found: C, 48.80; H, 6.92; N, 19.79.

5′-Deoxy-5′-S-(4-thiobutylamine)adenosine Sulfate.—The above isopropylidene nucleoside (1.6 g.) was dissolved in *N* sulfuric acid (20 ml.) and allowed to stand at room temperature for 24 hr. Paper chromatography showed that the product contained only traces of ultraviolet absorbing impurities. However, the oil resulting on addition of ethanol to the acid solution could not be induced to crystallize. This oil was taken up in water and an excess of a saturated aqueous solution of picric acid added. The precipitated picrate was filtered off, washed with a little water, and recrystallized twice from hot water; yield, 1.9 g.; m.p. 174–176° dec.

The purified picrate (1.6 g.) was dissolved in 50% aqueous dimethylformamide (100 ml.) and passed down a column (2 × 15 cm.) of Dowex 1 anion-exchange resin (acetate form, 100–200 mesh). The column was washed with water (100 ml.) and the combined eluate and washings evaporated to dryness *in vacuo*. The residue was taken up in alcohol (*ca.* 10 ml.) and transferred to a centrifuge tube. Sulfuric acid (2 *N*, 1 ml.) was added and the solid precipitate separated by centrifugation and washed with alcohol. The precipitate was redissolved in water, treated with a little decolorizing charcoal, and ethanol was then added to produce a slight opalescence in the solution. 5′-Deoxy-5′-S-(4-thiobutylamine)adenosine sulfate (238 mg.) crystallized slowly over several days, m.p. 166–169° dec., from aqueous ethanol.

Anal. Calcd. for $C_{14}H_{23}N_6O_3S \cdot 0.5\ SO_4$: C, 41.68; H, 5.74; N, 20.83. Found: C, 41.22; H, 5.83; N, 20.34.

2′,3′-Isopropylidene-5′-deoxy-5′-S-(2-thioethylamine)adenosine.—This compound was prepared by condensing the sodio derivative of 2-thioethylamine (cysteamine) (1.4 g.) in liquid ammonia with 2′,3′-isopropylidene-5′-toluene-*p*-sulfonyladenosine (9.2 g.).

After working up in the usual way a clear mobile oil (6.0 g.) was obtained which could not be induced to crystallize. It ran as a single compound in water-saturated butanol (R_f 0.64) and was homogeneous under ultraviolet light and to the ninhydrin and iodoplatinate sprays.

5′-Deoxy-5′-S-(2-thioethylamine)adenosine Bisulfate.—The above isopropylidene derivative (1.0 g.) was dissolved in *N* sulfuric acid (25 ml.) and left overnight at room temperature. The product (1.0 g.) was precipitated as its monohydrate by the addition of alcohol and recrystallized from aqueous alcohol; m.p. 188° dec.

Anal. Calcd. for $C_{12}H_{19}N_6O_3S \cdot HSO_4 \cdot H_2O$: C, 32.57; H, 5.01; N, 19.00; S, 14.49; wt. loss on drying, 4.07. Found: C, 32.75; H, 5.15; N, 19.44; S, 14.20; wt. loss (100° under high vacuum for 3 hr.), 3.75.

5′-Deoxy-5′-S-(3-methylthiopropylamine)sulfoniumadenosine ("Decarboxylated S-Adenosylmethionine").—5′-Deoxy-5′-S-(3-thiopropylamine)adenosine bisulfate (100 mg.) was dissolved in a mixture of equal parts of formic and acetic acids (5 ml.) and to this was added methyl iodide (0.5 ml.). The solution was left in the dark at room temperature for 6 days after which time it was diluted with an equal volume of water and extracted three times with 10-ml. portions of ether. A solution of flavianic acid (2% in *N* HCl, 10 ml.) was then added and the precipitated sulfonium flavianate centrifuged, washed with two 5-ml. portions of cold dilute flavianic acid and then with 5 ml. of cold water. The yield was 127 mg. after drying *in vacuo*. A small portion of the flavianate was rapidly recrystallized from hot water. It melted at 210–214° dec. and gave an analysis consistent with a diflavianate.

Anal. Calcd. for $C_{14}H_{22}N_6O_3S(C_{10}H_6N_2O_8S)_2$: C, 41.55; H, 3.49. Found: C, 41.55; H, 4.12.

The diflavianate was suspended in 0.4 *N* hydrochloric acid (10 ml.) and extracted with five to six 10-ml. lots of 2-butanone until the aqueous layer was colorless. The aqueous layer was extracted once with ether and then treated with sufficient Dowex 1 in the acetate form to remove chloride ions. The aqueous layer was then lyophilized and the residue taken up in a little water and adjusted to pH 5–6. The yield of sulfonium nucleoside was 146 μmoles (based on an extinction coefficient of 16,000 at 260 mμ). This material migrated towards the cathode at a rate of 3.6 cm./hr. when subjected to paper electrophoresis at pH 5.8 with a voltage gradient of 7 v./cm. It was homogeneous under the ultraviolet lamp (260 mμ) and to the ninhydrin, iodoplatinate, and periodate Schiff sprays.

The preparation of the corresponding 5′-deoxy-5′-S-(2-methylthioethylamine)- and (4-methylthiobutylamine)sulfoniumadenosine compounds and the precipitation and decomposition of their flavianates were carried out in a similar manner.

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Allylic Chlorides. XXVII. The Relative Reactivities of γ-Alkylallyl Chlorides

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Rate and thermodynamic data are presented for the reaction between both potassium iodide in acetone and sodium ethoxide in ethanol and the following allyl chlorides: allyl chloride, *cis*- and *trans*-γ-methylallyl chloride, *cis*- and *trans*-γ-ethylallyl chloride, *cis*- and *trans*-γ-isopropylallyl chloride. All of the γ-alkylallyl chlorides were more reactive than allyl chloride and the *cis* isomer was more reactive than the *trans* isomer, especially with potassium iodide. The reasons for this configurationally related difference in reaction rate is not clear.

During the course of an extended investigation of allylic chlorides their relative reactivities toward potassium iodide in acetone and sodium ethoxide in ethanol were obtained by comparing their rate constants with that of allyl chloride. Thermodynamic data for the reactions of allyl chloride, and of γ-methyl-, γ-ethyl-, and γ-isopropylallyl chlorides have now been obtained. Similar data were reported previously for the 1-chloro-4,4-dimethyl-2-pentenes (γ-*t*-butylallyl chloride).[1]

The γ-alkylallyl chlorides were prepared in a manner similar to that used for the synthesis of the 1-chloro-4,4-dimethyl-2-pentenes.[1] Table I contains the boiling points or boiling ranges, densities, and refractive indices of the chlorides and their alcohol precursors. The isomers were characterized by their physical constants, infrared spectra, g.l.c. analyses, and elemental anal-

(1) L. F. Hatch, H. D. Weiss, and T. P. Li, *J. Org. Chem.*, **26**, 61 (1961).