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Improved Synthesis of Decarboxylated *S*-Adenosylmethionine and Related Sulfonium Compounds

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Decarboxylated *S*-adenosyl-L-methionine and its nine analogs have been prepared by a modified method of Jamieson including alkylation of the appropriate aminoalkyladenosyl thioether with alkyl iodides in a mixture of formic and acetic acids in the presence of silver perchlorate. The use of silver perchlorate allowed various combinations of the thioether and the alkyl iodide, and prompted the reaction. The sulfonium compounds were obtained as a white hygroscopic powder in 99% ethanol after purification by silica gel column chromatography with a solvent system of butanol–acetic acid–water (1:1:1). The chemical and physical data of the sulfonium compounds supported a general structure containing 2 mol of sulfuric acid and 0.5 mol of ethanol. The nuclear magnetic resonance data showed the existence of sulfonium diastereoisomers.

Keywords——polyamine; silver perchlorate; *S*-adenosylmethionine; *S*-adenosylmethionine decarboxylase; spermidine synthase; spermine synthase; sulfonium synthesis; diastereoisomer

S-Adenosyl-L-methionine (SAM) is an essential substrate in both enzymatic transmethylation reaction and polyamine biosynthesis. Many works have been reported on the syntheses of its structural analogs and related compounds, although most of them are rather concerned with interactions to methyl transferases[2–5)] than to spermidine and spermine synthases.[6–8)] It is well known that SAM is decarboxylated by *S*-adenosyl-L-methionine decarboxylase to produce *S*-5'-deoxyadenosyl-(5')-3-methylthiopropylamine (decarboxylated *S*-adenosylmethionine; IIc), which is the donor of the propylamine moiety to putrescine or spermidine, yielding spermidine or spermine, respectively, and a limited substrate to a certain methyl transferase.[3)] IIc is not known to participate as an aminopropyl donor in any other biochemical pathways. Therefore, studies with IIc instead of SAM would bring problems of polyamine into focus. In a study of substrate specificity of spermidine synthase, we needed a series of this type of sulfonium compounds. Synthetic procedures of IIc and its two analogs have been reported by Jamieson,[6)] with incomplete descriptions about chemical and physical data of the final sulfonium compounds because of failure to crystallize them.

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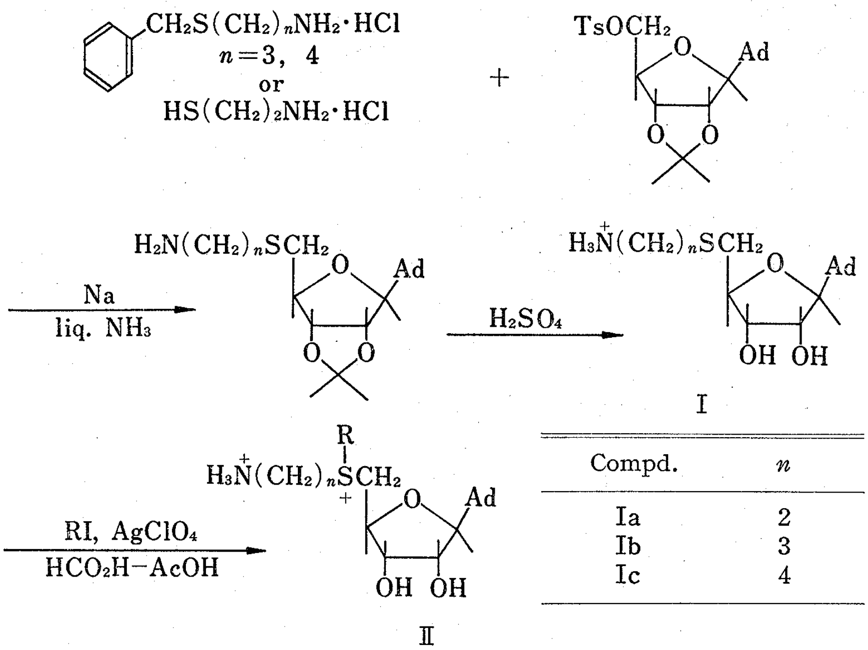

Compd.	n
Ia	2
Ib	3
Ic	4

Compd.	n	R	Compd.	n	R
IIa	2	CH_3	IIf	3	$(CH_2)_3CH_3$
IIb	2	CH_2CH_3	IIg	3	CH_2CO_2H
IIc	3	CH_3	IIh	3	CH_2CONH_2
IId	3	CH_2CH_3	IIi	3	$(CH_2)_2CO_2H$
IIe	3	$(CH_2)_2CH_3$	IIj	4	CH_3

Chart 1

Scheme of the syntheses mostly followed the procedure of Jamieson[6] except a part of the sulfonium synthesis (Chart 1). 2′,3′-O-Isopropylidene-5′-*S*-thioalkylamineadenosine was prepared by condensation of benzylthio-*n*-alkylamine hydrochloride and 2′,3′-O-isopropylidene-5′-O-*p*-toluenesulfonyladenosine in liquid ammonia and metallic sodium. The isopropylidene group was then removed by hydrolysis with 1 N sulfuric acid at room temperature overnight. The corresponding thioether (I) was alkylated to the sulfonium compound (II) with the appropriate alkyl iodide and silver perchlorate in a mixture of equal parts of formic and acetic acids. The general procedure of this alkylation previously described by Jamieson contained no use of silver perchlorate, and has been adopted to synthesize SAM analogs with minor modifications in the most recent reports.[4,5,8] However, it is time-consuming, such as 6 days of reaction time, and is applicable only to the methylation, since other alkyl iodides (*e.g.* ethyl, propyl, butyl, *etc.*) have little or no reactivity under the condition described. In addition, we encountered unsatisfactory reactivity of methyl iodide with *S*-5′-deoxyadenosyl-(5′)-2-thioethylamine (Ia) to synthesize the sulfonium compound (IIa). The reaction, after a prolonged reaction time of a month, proceeded in about 50% or less judged from ultraviolet absorption on thin layer chromatogram, accompanying with an increase of unfavourable colored substances which disturbed purification of IIa, whereas the present silver assisted reaction proceeded in almost 100% at room temperature overnight.

The reactivity in the alkylation was markedly influenced both by the structure of the thioether and by the alkyl iodide used. Increasing number of methylene group of the thioether (*n*) facilitated formation of the corresponding sulfonium compounds, while increasing molecular weight of alkyl iodides decreased the formation. In the alkylation of *S*-5′-deoxyadenosyl-(5′)-3-thiopropylamine (Ib) with a series of alkyl iodides such as methyl, ethyl, propyl, and butyl iodides, their reactivities were roughly measured by ultraviolet absorption of the corresponding sulfonium compounds, IIc, IId, IIe, and IIf on thin layer chromatogram. Ib changed almost completely to IIc after 3 hr of reaction time, and in 70% to IId after 3 hr, and in 80% after 16 hr with complete disappearance of Ib and appearance of unknown substances having *Rf* values higher than Ib. IIe and IIf were obtained in 60% and 50% yield after 16 hr respectively with unreacted Ib and unknown substances. In case of butyl iodide, the alkylation seemed to be hindered by the decrease of its solubility in the mixture of acids. Isobutyl iodide did not react with Ib under the present condition. A possible explanation for this is a rapid conversion of isobutyl iodide to isobutene due to a forced removal of iodide by silver. Other alkyl iodides so far tested, including iodoacetic acid, iodoacetamide, and iodopropionic acid, similarly reacted with Ib to give the corresponding sulfonium compounds with reasonable yields.

The amounts of by-products obviously increased with additional silver perchlorate, so that further alkylation might occur in a different part of the molecule. Hence, the molar ratio of silver perchlorate to I was chosen as 2 to 1. Optimal ratio differed for each combination of I and alkyl iodides. When methyl iodide was used, the reaction proceeded almost quantitatively, and the amount of silver perchlorate could be reduced to a slight excess over the equivalent amount of I. In the present procedure, we used a large excess of alkyl iodide (*i.e.* 40 times as much as I) based on the procedure of Jamieson. This amount could be reduced to some extent, but we have used the recipe to obtain a high yield.

Occurrence of unreacted thioether and by-products under the present reaction condition required purification procedure for the sulfonium compound. II in the reaction mixture forms mixed salts with various anions such as HSO_4^-, ClO_4^-, HCO_2^-, and $CH_3CO_2^-$, and the mixed salts are fairly soluble in alcoholic solvent. This is different from particular insolubility of sulfuric acid salt of II to alcoholic solvent. Thus, we applied a solvent system containing butanol, which was successfully used in thin layer chromatography (TLC), to silica gel column chromatography, and found it effective for the purification. In the column chromatography, the unknown by-products and unreacted I eluted nearly to the solvent front, and thereafter II as a broad band, being well separated from other trace amounts of ultraviolet absorbing compounds with lower *Rf* values. Trace silver iodide contaminated was retained on the column. After the solvent was removed, the residue containing II was dissolved in a small volume of 1 N sulfuric acid to make hydrogen sulfate form. Then, excess amount of ethanol was added to the acid solution to precipitate an oily II. This treatment was usually repeated several times to attain its complete sulfuric acid form. The oily II never crystallized in the alcoholic solvent containing water, solidified to a powder in 99% ethanol. The hygroscopic powder was well characterized as sulfonium compound by chemical and physical ways.

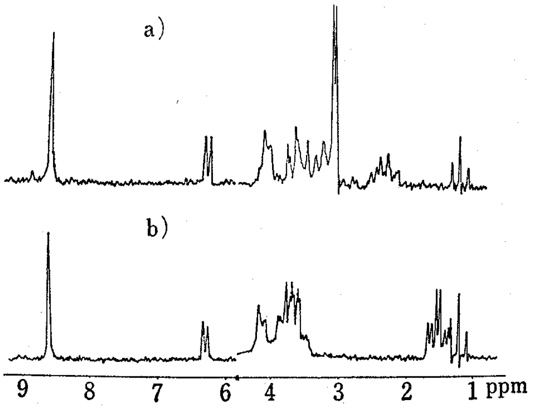

Fig. 1. NMR Spectra of IIc (a), IIb (b)

The nuclear magnetic resonance (NMR) spectrum of IIc is shown in Fig. 1a. The triplet signals appeared at 1.2 ppm suggested the existence of hardly volatile ethanol in the molecule, being consistent with the assigned structure containing 2 mol of sulfuric acid and 0.5 mol of ethanol by elemental analysis. The signals appeared at 3.04 and 3.07 ppm were attributed to the methyl group at the sulfonium center. The NMR spectrum of IIb is an another example as shown in Fig. 1b. The methyl signals of ethylsulfonium group were equally divided. These are good demonstrations for the existence of sulfonium diastereoisomers. It is certain from the well-known stereoisomerism about triply substituted sulfonium atoms that the other sulfonium compounds presently synthesized are also diastereomers at the sulfonium pole.

Studies are now undergoing in our labolatory to evaluate the synthesized IIc and its analogs as substrates, inhibitors or activators for a rat prostate spermidine synthase.

Experimental

Elemental analyses were conducted by Analytical Division of Chugai Co. TLC was carried out on silica gel HF_{254} (Typ 60) (E. Merck) with a solvent system of $BuOH–AcOH–H_2O$ (3: 2: 2). The spots were detected by visual examination under UV light, 254 nm. All these data are summarized in Table I. All melting points were uncorrected. NMR data were recorded on a Hitachi Perkin Elmer R-20A spectrometer (60 MHz), and IR data on a Hitachi 285 spectrophotometer.

Table I. Elemental analyses and *Rf* values of synthetic compounds

Compd. No.	*Rf*[a]	Formula	Analysis (%)					
			Calcd.			Found		
			C	H	N	C	H	N
Ia	0.60	$C_{12}H_{19}N_6O_3S \cdot HSO_4 \cdot 1/2H_2O$	33.25	4.88	19.39	33.33	4.73	19.31
Ib	0.63	$C_{13}H_{21}N_6O_3S \cdot HSO_4 \cdot 1/2H_2O$	34.89	5.18	18.78	34.75	5.25	18.62
Ic	0.64	$C_{14}H_{23}N_6O_3S \cdot HSO_4 \cdot 1/2H_2O$	36.44	5.46	18.21	36.57	5.29	18.16
IIa	0.22	$C_{13}H_{22}N_6O_3S \cdot 2HSO_4 \cdot 1/2EtOH$	30.05	4.86	15.02	29.92	4.75	15.22
IIb	0.19	$C_{14}H_{24}N_6O_3S \cdot 2HSO_4 \cdot 1/2EtOH$	31.41	5.10	14.65	31.25	4.77	14.40
IIc	0.21	$C_{14}H_{24}N_6O_3S \cdot 2HSO_4 \cdot 1/2EtOH$	31.41	5.10	14.65	31.44	5.11	14.95
IId	0.19	$C_{15}H_{26}N_6O_3S \cdot 2HSO_4 \cdot 1/2EtOH$	32.70	5.32	14.30	32.67	5.38	14.29
IIe	0.25	$C_{16}H_{28}N_6O_3S \cdot 2HSO_4 \cdot 1/2EtOH$	33.94	5.53	13.97	33.91	5.61	13.74
IIf	0.31	$C_{17}H_{30}N_6O_3S \cdot 2HSO_4 \cdot 1/2EtOH$	35.11	5.73	13.65	35.06	5.96	13.36
IIg	0.30	$C_{15}H_{24}N_6O_5S \cdot 2HSO_4 \cdot 1/2EtOH$	31.12	4.73	13.61	31.21	4.51	13.30
IIh	0.27	$C_{15}H_{25}N_7O_4S \cdot 2HSO_4 \cdot 1/2EtOH$	31.16	4.90	15.90	29.60	4.37	15.89
IIi	0.27	$C_{16}H_{26}N_6O_5S \cdot 2HSO_4 \cdot 1/2EtOH$	32.33	4.95	13.30	32.47	4.76	13.19
IIj	0.16	$C_{15}H_{26}N_6O_3S \cdot 2HSO_4 \cdot 1/2EtOH$	32.70	5.32	14.30	32.87	5.12	14.26

[a] Silica gel TLC with a solvent system of $BuOH–AcOH–H_2O$ (3: 2: 2).

S-5′-Deoxyadenosyl-(5′)-2-thioethylamine (Ia) hydrogen sulfate, *S*-5′-deoxyadenosyl-(5′)-3-thiopropylamine (Ib) hydrogen sulfate, and *S*-5′-deoxyadenosyl-(5′)-4-thiobutylamine (Ic) hydrogen sulfate were prepared by the literature procedures[6] with a slight modification for Ic. The purification steps for Ic through picrate and Dow 1 column chromatography were omitted, because an oily Ic hydrogen sulfate easily solidified in 99% ethanol. The intermediate aminothiols were used as hydrochlorides of their *S*-benzyl derivatives except in the case of 2-thioethylamine hydrochloride commercially available. The another intermediate 2′,3′-O-isopropylidene-5′-O-*p*-toluenesulfonyladenosine was synthesized by tosylation[9] of 2′,3′-O-isopropylideneadenosine obtained from Sigma. All chemical and physical data for Ia, Ib, and Ic agreed with those of the literature.

Synthesis and Purification of II——I hydrogen sulfate (1 mmol) was dissolved in a mixture of equal parts of formic and acetic acids (20 ml) in a brown glass vessel with stopper, and to this was added alkyl iodide (40 mmol). Silver perchlorate (2 mmol) dissolved in the same acid mixture in a concentration of 10% (w/v) was then added to the reaction mixture. Silver iodide precipitated rapidly in order of reactivities of alkyl iodides. After standing overnight in the dark at room temperature, the mixture was centrifuged to remove silver iodide, and the supernatant added with 25 ml of water was extracted with 50 ml of ether and twice with 25 ml. The resulting aqueous phase was lyophilized. The residue was dissolved in 2 to 4 ml each of water, acetic acid, and BuOH, to become clear solution in $BuOH–AcOH–H_2O$ (1: 1: 1). The solution was subjected to the following column chromatography. Silica gel (Wako gel C-200) (30 g) was suspended in the solvent system of $BuOH–AcOH–H_2O$ (1: 1: 1), and fines were removed several times by decantation. The column (18 mm i.d. × 26 cm) was well washed with 500 ml of the solvent. The sample solution was then applied to the column, and the column was eluted with the same solvent. Fractions of 10 ml were collected. The first ultraviolet absorbing fractions were near the void volume, and then the second fractions of eluate

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9) W. Sakami, "Biochemical Preparations," Vol. 8, ed. by A. Meister, John Wiley and Sons, Inc., New York, 1961, p. 5.

containing II with an approximate volume of 100 to 200 ml. The eluate was evaporated to dryness *in vacuo* at less than 30°. The residue was dissolved in 2 ml of 1 N H_2SO_4, and the solution was transferred to a 50 ml-centrifuge tube, and to the solution 30 ml of ethanol was added. An oily precipitate was separated by centrifugation at 0°. This treatment was repeated three times and twice with water instead of 1 N H_2SO_4. Finally the oily precipitate solidified in 99% ethanol. The solid sticked on inside wall of the centrifuge tube was scraped off with a glass rod to a powder. The white hygroscopic powder was collected, washed with ethanol and dried over P_2O_5 *in vacuo* at room temperature for two days. IR data were not characteristic for a series of these sulfonium compounds.

***S*-5′-Deoxyadenosyl-(5′)-2-methylthioethylamine (IIa)**——To a mixture of Ia hydrogen sulfate (435 mg, 1 mmol) and MeI (2.49 ml, 40 mmol) in 20 ml of HCO_2H–AcOH (1 : 1), 4.2 ml of $AgClO_4$ solution (100 mg/ml of HCO_2H–AcOH) was added. After treatments by the general procedure described above, a yield of 297 mg (54%) of the desired IIa dihydrogen sulfate was obtained. mp 143—145° (dec.). IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 620, 1110, 1690, 3400. NMR (D_2O) δ: 1.20 (3/2H, t, 7 Hz), 3.11 and 3.16 (3H, s), 3.41—4.00 (5H, m), 4.13 (2H, b.d.), 4.5—5.1 (3H, m), 6.29 (1H, d, 4Hz), 8.59 (2H, s).

***S*-5′-Deoxyadenosyl-(5′)-2-ethylthioethylamine (IIb)**——To a mixture of Ia hydrogen sulfate (435 mg, 1 mmol) and EtI (3.2 ml, 40 mmol) in 20 ml of HCO_2H–AcOH, 4.2 ml of the $AgClO_4$ solution was added. After treatments by the general procedure, a yield of 160 mg (28%) of the desired IIb di-hydrogen sulfate was obtained. mp 138—141° (dec.). IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 620, 1110, 1690, 3410. NMR (D_2O) δ: 1.19 (3/2H, t, 7 Hz), 1.47 and 1.52 (3H, t, 7 Hz), 3.37—3.87 (7H, m), 4.09 (2H, b.d.), 4.5—5.1 (3H, m), 6.26 (1H, d, 4 Hz), 8.57 (2H, s).

***S*-5′-Deoxyadenosyl-(5′)-3-methylthiopropylamine (IIc)**——To a mixture of Ib hydrogen sulfate (448 mg, 1 mmol) and MeI (2.49 ml, 40 mmol) in 20 ml of HCO_2H–AcOH, 4.2 ml of the $AgClO_4$ solution was added. After treatments by the general procedure, a yield of 385 mg (67%) of the desired IIc di-hydrogen sulfate was obtained. mp 149—151° (dec.).

This reaction completed after 3 hr with still precipitating AgI. When the reaction was stopped at this time by the ether extraction, the column chromatography could be omitted. AgI was carefully removed by centrifugation, and IIc di-hydrogen sulfate was obtained in 80% yield. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 621, 1110, 1687, 3360. NMR (D_2O) δ: 1.20 (3/2H, t, 7 Hz), 2.33 (2H, m), 3.04 and 3.07 (3H, s), 3.16—3.78 (5H, m), 4.04 (2H, b.d.), 4.5—5.1 (3H, m), 6.25 (1H, d, 4.2 Hz), 8.56 (2H, s).

***S*-5′-Deoxyadenosyl-(5′)-3-ethylthiopropylamine (IId)**——To a mixture of Ib hydrogen sulfate (300 mg, 0.67 mmol) and EtI (2.15 ml, 26.9 mmol) in 13.4 ml of HCO_2H–AcOH, 280 mg (1.35 mmol) of $AgClO_4$ was added. After treatments described above, a yield of 215 mg (37%) of the desired IId di-hydrogen sulfate was obtained. mp 148—150° (dec.). IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 621, 1115, 1688, 3400. NMR (D_2O) δ: 1.20 (3/2H, t, 7 Hz), 1.46 and 1.47 (3H, t, 7 Hz), 2.32 (2H, m), 3.00—3.77 (7H, m), 4.04 (2H, b.d.), 4.5—5.1 (3H, m), 6.26 (1H, d, 4.4 Hz), 8.56 (2H, s).

***S*-5′-Deoxyadenosyl-(5′)-3-propylthiopropylamine (IIe)**——To a mixture of Ib hydrogen sulfate (448 mg, 1 mmol) and PrI (3.9 ml, 40 mmol) in 20 ml of HCO_2H–AcOH, 4.2 ml of the $AgClO_4$ solution was added. After treatments described above, a yield of 236 mg (39%) of the desired IIe di-hydrogen sulfate was obtained. mp 149—151° (dec.). IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 610, 1110, 1690, 3410. NMR (D_2O) δ: 0.96 and 0.98 (3H, t, 7 Hz), 1.18 (3/2H, t, 7 Hz), 1.81 (2H, m), 2.29 (2H, m), 3.00—3.87 (7H, m), 4.00 (2H, b.d.), 4.5—5.1 (3H, m), 6.23 (1H, d, 4 Hz), 8.54 (2H, s).

***S*-5′-Deoxyadenosyl-(5′)-3-butylthiopropylamine (IIf)**——To a mixture of Ib hydrogen sulfate (448 mg, 1 mmol) and BuI (4.6 ml, 40 mmol) in 20 ml of HCO_2H–AcOH, 4.2 ml of the $AgClO_4$ solution was added, and the reaction mixture was stirred overnight as described above, to prevent separation of BuI. The purification steps were similar as described above. A yield of 247 mg (40%) of the desired IIf di-hydrogen sulfate was obtained. mp 149—151° (dec.). IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 610, 1110, 1690, 3400. NMR (D_2O) δ: 0.78 and 0.83 (3H, t, 7 Hz), 1.21 (3/2H, t, 7 Hz), 1.20—2.08 (4H, m), 2.32 (2H, m), 3.03—3.92 (7H, m), 4.03 (2H, b.d.), 4.5—5.1 (3H, m), 6.28 (1H, d, 4 Hz), 8.59 (2H, s).

***S*-5′-Deoxyadenosyl-(5′)-3-carboxymethylthiopropylamine (IIg)**——To a mixture of Ib hydrogen sulfate (224 mg, 0.5 mmol) and ICH_2CO_2H (3.7 g, 20 mmol) in 10 ml of HCO_2H–AcOH, 2.1 ml of the $AgClO_4$ solution was added. After treatments described above, a yield of 157 mg (50%) of the desired IIg di-hydrogen sulfate was obtained. Solubility of IIg to BuOH–AcOH–H_2O (1 : 1 : 1) was markedly low, and so the column chromatographic purification seemed to be inadequate for preparative purpose. A higher yield would be expected if the chromatographic purification step was omitted as described in IIc. mp 145—147° (dec.). IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 620, 1115, 1690, 3420. NMR (D_2O) δ: 1.19 (3/2H, t, 7 Hz), 2.32 (2H, m), 3.04—3.35 (2H, m), 3.44—3.78 (3H, m), 4.03 (2H, b.d.), 4.5—5.1 (3H, m), 6.24 (1H, d, 4 Hz), 8.54 (2H, s).

***S*-5′-Deoxyadenosyl-(5′)-3-carbamoylmethylthiopropylamine (IIh)**——To a mixture of Ib hydrogen sulfate (200 mg, 0.45 mmol) and ICH_2CONH_2 (3.3 g, 18 mmol) in 8 ml of HCO_2H–AcOH, 1.8 ml of the $AgClO_4$ solution was added. The column chromatography was omitted in this case. In the extraction procedure, water insoluble precipitate was observed. This is probably a contamination of large excess of iodoacetamide, and was removed by centrifugation. Yield of IIh dihydrogen sulfate was about 200 mg (72%). mp 142—145° (dec.). The data of elemental analysis are still unsatisfactory, but NMR data prove the structure of

IIh. IR ν_{max}^{KBr} cm^{-1}: 620, 1100, 1690, 3390. NMR (D_2O) δ: 1.18 (3/2H, t, 7 Hz), 2.35 (2H, m), 3.08—3.40 (2H, m), 3.55—3.87 (3H, m), 4.15 (2H, b.d.), 4.5—5.1 (3H, m), 6.24 (1H, d, 3.8 Hz), 8.54 (2H, s).

***S*-5′-Deoxyadenosyl-(5′)-3-carboxyethylthiopropylamine (IIi)**——To a mixture of Ib hydrogen sulfate (200 mg, 0.45 mmol) and $ICH_2CH_2CO_2H$ (3.6 g, 18 mmol) in 8 ml of HCO_2H–AcOH, 1.8 ml of the $AgClO_4$ solution was added, and the reaction mixture was allowed to stand for 2 days at room temperature in the dark. About 60% of the ultraviolet absorbing compounds was IIi from the spot located at *Rf* value of 0.27 on TLC. The compound was purified by the column chromatography. The final yield was not calculated. mp indefinite. IR ν_{max}^{KBr} cm^{-1}: 618, 1100, 1680, 3400. NMR (D_2O) δ: 1.19 (3/2H, t, 7 Hz), 2.36 (2H, m), 2.79—3.39 (4H, m), 3.49—3.88 (5H, m), 4.10 (2H, b.d.), 4.5—5.1 (3H, m), 6.24 (1H, d, 3 Hz), 8.56 (2H, s).

***S*-5′-Deoxyadenosyl-(5′)-4-methylthiobutylamine (IIj)**——To a mixture of Ic hydrogen sulfate (231 mg, 0.5 mmol) and MeI (1.25 ml, 20 mmol) in 10 ml of HCO_2H–AcOH, 2.1 ml of the $AgClO_4$ solution was added, and the reaction mixture was allowed to stand for 1.5 hr at room temperature in the dark. The reaction completed with still precipitating AgI. After the ether extraction, the aqueous phase was centrifuged to remove newly precipitated AgI. To the clear solution, 1 ml of 1 N H_2SO_4 and excess ethanol was added to precipitate oily IIj di-hydrogen sulfate. The precipitate was dissolved in 2 ml of 1 N H_2SO_4, and to the solution 40 ml of ethanol was added. This treatment was repeated three times and twice with 2 ml of water. Finally IIj di-hydrogen sulfate solidified in 99% ethanol as described above. The yield was 253 mg (86%). mp 151—153° (dec.). IR ν_{max}^{KBr} cm^{-1}: 618, 1107, 1687, 3390. NMR (D_2O) δ: 1.23 (3/2H, t, 7 Hz), 1.76—2.13 (2H, m), 3.07 and 3.09 (3H, s), 3.43—4.00 (5H, m), 4.10 (2H, b.d.), 4.6—5.2 (3H, m), 6.43 (1H, d, 4 Hz), 8.80 (2H, s).

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