This solution was concentrated *in vacuo* to an oily residue which upon trituration with ethanol gave 5.4 g of crude dimer **6**.

Two recrystallizations from 95% ethanol afforded 3.0 g of pure dimer **6** as its dihydrochloride: mp 194–197°; equiv wt, 204 (calcd 196); nmr and uv spectra as given in Tables II and III; blue color with 2,6-dichloroquinone chlorimide (Gibbs test).[2]

Anal. Calcd for $C_{16}H_{20}N_2O_5 \cdot 2HCl$: C, 48.86; H, 5.64; N, 7.12; Cl, 18.03. Found: C, 48.46; H, 5.70; N, 6.85; Cl, 18.43.

Under these same conditions pyridoxol-4,5-diacetate[11] was converted quantitatively in to pyridoxol hydrochloride.

Methiodide of Dimer 6.—A mixture of 100 mg of dimer **6**, 5 ml of methyl alcohol, 5 ml of methyl iodide, and 10 ml of benzene was heated at 50° for 20 hr, then concentrated to dryness. The crude methiodide exhibited in pH 7 borate buffer an absorption maximum at 310 nm ($E^{1\%}_{1cm}$ 307).

Compound 9.—Ten grams (0.0334 mol) of crude adduct **3** and 17.7 g (0.186 mol) of 3-hydroxypyridine was stirred in 250 ml of acetic acid 0.4 *M* in water at room temperature for 18 hr. The reaction mixture was concentrated, diluted with 100 ml of 2.3 *N* hydrochloric acid, heated at 95° for 2.5 hr, treated with 1.4 g of Darco KB charcoal at 95° for 2 hr, and filtered. The filtrate was charged to 200 g of Amberlite IR-120 resin on the hydrogen cycle. Excess 3-hydroxypyridine was eluted with 2 *N* hydrochloric acid, the column was washed to neutrality with water, and the product was eluted with 1 l. of 2 *N* ammonia water. This eluate was concentrated to dryness *in vacuo*, affording 6.0 g (77%) of solid compound **9**, single spot by tlc, which was converted into its dihydrochloride in ethanolic hydrogen chloride and recrystallized from aqueous ethanol, mp 191–192°; uv and nmr spectra are in the tables.

Anal. Calcd for $C_{13}H_{14}N_2O_3 \cdot 2HCl$: C, 48.91; H, 5.05; N, 8.78. Found: C, 48.87; H, 5.08; N, 9.06.

Registry No.—**3**, 19206-42-9; **5**·HCl, 58-56-0; **5**·HCl 4-methyl ether, 3131-27-9; **6**, 19203-53-3; **6**·2HCl, 19598-93-7; **6** methiodide, 19245-01-3; **9**, 19203-54-4; **9**·2HCl, 19598-94-8; **11**, 19203-56-6.

(11) S. A. Harris, *J. Amer. Chem. Soc.*, **62**, 3203 (1940).

The Base Cyclization of *trans*-S-(1-Butenyl)-L-cysteine S-Oxide

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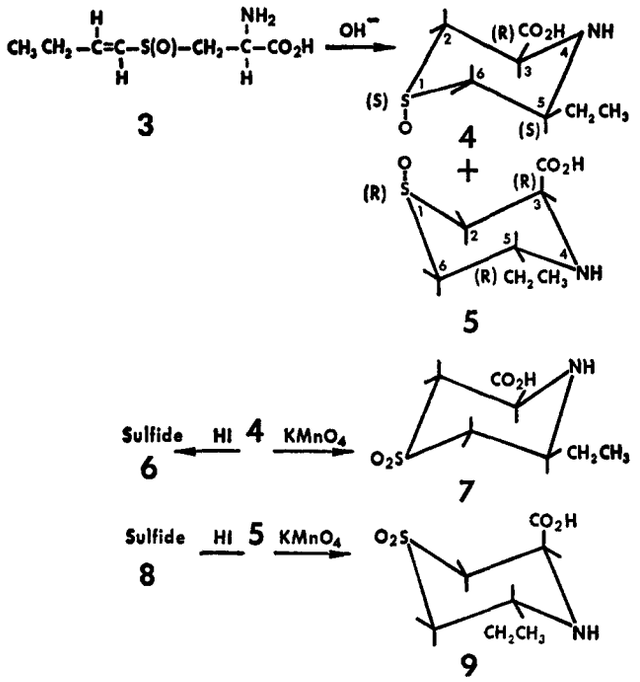
trans-S-(1-Propenyl)-L-cysteine S-oxide, the naturally occurring flavor precursor in the onion,[2] cyclizes in aqueous base to give cycloalliin[3] (**1**) in high yield as the only isolable product. The corresponding *cis* compound,[4] however, under the same conditions yields cycloalliin (**1**) and an isomeric cyclic sulfoxide[5] **2**. We now report that *trans*-S-(1-butenyl)-L-cysteine S-oxide (**3**) cyclizes in an analogous manner to give the isomeric cyclic sulfoxides **4** and **5** (Scheme I).

trans-S-(1-Butenyl)-L-cysteine S-oxide (**3**) was prepared by oxidation of the corresponding sulfide with hydrogen peroxide in aqueous solution. The oxidation

SCHEME I



product could not be separated into the two diastereomers, but a fairly pure sample of the dextrorotatory sulfoxide, $[\alpha]^{25}D$ +61° (water), was obtained in small yields.[7] A solution of the mixed sulfoxides **3** in 2 *N* ammonium hydroxide after 5–7 days at room temperature yielded 13% 3-(*R*)-carboxy-5-(*S*)-ethyl-1,4-thiazane S-oxide (**4**) and 30% 3-(*R*)-carboxy-5-(*R*)-ethyl-1,4-thiazane S-oxide (**5**).

The structures of the new compounds and configuration at C-5 were established by oxidation of the cyclic sulfoxides to sulfones of known configuration[6] previously established by nmr. Oxidation of **4** yielded a sulfone identical with **7** which establishes the (*S*) configuration for C-5.[8] Similarly, isomer **5** by oxidation is correlated with sulfone **9** and therefore the configuration of C-5 is (*R*).

Evidence that the sulfoxide in **4** is axial and therefore (*S*) as in cycloalliin follows from a comparison of the D-line rotational changes on reduction of sulfoxide to sulfide. When **4** is reduced to the sulfide **6** by hydriodic acid, the molecular rotation in acid decreases in a positive sense: $[M]D$ −43.4° (3 *N* hydrochloric acid) for sulfoxide → $[M]D$ −59.2° (3 *N* hydrochloric acid) for sulfide. Conversion of cycloalliin to its sulfide in the same manner results in a change in the same direction: $[M]D$ −19° (hydrochloric acid) for cycloalliin → $[M]D$ −38.5° for sulfide. Rotational changes in water were also both in the same direction. Since no drastic ring conformational changes are expected in these reactions, the configuration of the sulfoxide in **4** should be the same as in cycloalliin.

By a similar argument the sulfoxide of **5** is axial with the (*R*) configuration. Thus, reduction of sulfoxide **5** to sulfide **8** is accompanied by an increase

(1) A Laboratory of the Western Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture.

(2) A. I. Virtanen and C. G. Spåre, *Suomen Kemistilehti*, *B*, **34**, 72 (1961).

(3) A. I. Virtanen and E. J. Matikkala, *Acta Chem. Scand.*, **13**, 623 (1959).

(4) J. F. Carson and Lois E. Boggs, *J. Org. Chem.*, **31**, 2862 (1966).

(5) Cycloalliin (**1**) and its isomer **2** are the methyl homologs of **4** and **5**, respectively.[6]

(6) J. F. Carson, L. Boggs, and R. E. Lundin, *J. Org. Chem.*, **33**, 3739 (1968).

(7) A. L. Müller and A. I. Virtanen, *Acta Chem. Scand.*, **20**, 1163 (1966), prepared the sulfoxide by oxidation of the cysteine derivative with perbenzoic acid and apparently experienced similar difficulties in isolating a pure product. These investigators failed to isolate cyclization products from reaction of their sulfoxide preparation in ammoniacal solution.

(8) C-3 is known to be (*R*) in both isomers because of their formation from a derivative of L-cysteine.

TABLE I

NMR SPECTRAL DATA[a] FOR 3-(*R*)-CARBOXY-5-(*R*)-ETHYL-1,4-THIAZANE S-(R)-OXIDE (**5**) IN TFA–20% D_2O AT 65° AND 3-(*R*)-CARBOXY-5-(*R*)-METHYL-1,4-THIAZANE S-(*R*)-OXIDE (**2**) IN TFA AT 60°

	5		**2**	
Proton	δ'[b]	*J*, Hz	δ[c]	*J*, Hz
CH_3	0.69 t	J 7.51	0.88 d	J 6.8
H-6(a)	2.61 d of t	$J_{66'}$ 15.2 (g)	2.43 q	$J_{66'}$ 15.4 (g)
		J_{56} 11.8 (aa)		J_{56} 11.2 (aa)
H-6(e)	2.98 d of t	$J_{66'}$ 15.0 (g)	2.68 d of t	$J_{66'}$ 15.4 (g)
		J_{56} 2.5 (ae)		J_{56} 2.5 (ae)
		J_{26} 2.5 (lr)		J_{26} 2.5 (lr)
H-5(a)	4.00 m		4.00 m	
H-2(a)	2.91 q	$J_{22'}$ 15.4 (g)	2.69 q	$J_{22'}$ 15.8 (g)
		J_{23} 5.7 (ae)		J_{23} 5.5 (ae)
H-2(e)	3.57 d of t	$J_{22'}$ 15.4 (g)	3.35 d of t	$J_{22'}$ 15.8 (g)
		J_{23} 2.7 (ee)		J_{23} 2.5 (ee)
		J_{26} 2.7 (lr)		J_{26} 2.5 (lr)
H-3(e)	4.31 q	J_{23} 5.7 (ae), 2.7 (ee)	4.16 q	J_{23} 5.5 (ae), 2.5 (ee)

[a] Obtained at 100 MHz: d = doublet, t = triplet, q = quartet, d of t = doublet of triplets, m = multiplet, g = *gem*, lr = long range. [b] Chemical shifts for **5** are in parts per million downfield from pivalic acid. [c] Chemical shifts for **2** are in parts per million downfield from tetramethylsilane.

in rotation in the positive sense: $[M]_D$ −126.6° (hydrochloric acid) for sulfoxide → $[M]_D$ −97.3° for sulfide. Reduction of the cycloalliin isomer **2** yielded a rotational change in the same direction: $[M]_D$ −144° (hydrochloric acid) for sulfoxide → $[M]_D$ −113° for sulfide. The argument is more doubtful in this case since a ring inversion could conceivably occur during reduction to sulfide for one sulfoxide and not for the other. However, the good agreement in the changes in molecular rotation (+29.3° for **5** → **8** and +31° for reduction of **2**) strengthens the applicability of the principle to this case.

That sulfoxide **5** has the same ring conformation, at least in trifluoroacetic acid (TFA), as the cycloalliin isomer **2** was shown by nmr. Table I shows spectral data for the two compounds. The large coupling constants, J_{56} = 11.8 Hz for **5** and 11.2 Hz for **2**, require a *trans*-diaxial relation between the C-5 proton and one C-6 proton in each compound. The coupling constants between the C-2 and C-3 protons, J_{23} = 5.7 and 2.7 Hz for **5** and J_{23} = 5.5 and 2.5 Hz for **2**, require that no diaxial relation can exist between C-2 and C-3 protons in each case, in agreement with the assigned conformations in TFA.

Experimental Section[9]

***trans*-S-(1-Butenyl)-L-cysteine S-Oxide (3).**—An aqueous solution of 2.57 g (0.0147 mol) of *trans*-S-(1-butenyl)-L-cysteine was oxidized with hydrogen peroxide as previously described.[4] Concentration of the oxidation solution to *ca.* 20 ml yielded 360 mg of cystine, apparently a decomposition product since the cystine content of the original amino acid was 1%. Occasionally, the yield of cystine reaches 25%. The solution, freed of cystine, upon the addition of acetone (8:1) yielded 1.78 g of amorphous product. Four recrystallizations from acetone–water yielded 147 mg of the (+) isomer as very fine crystals: mp 119–121° dec; rotation unchanged on recrystallization; $[\alpha]^{25}_D$ +61.2° (*c* 1.8, water); relative R_f with respect to alanine, 1.88; ir, 1580 (ionized carboxyl), 1030 (sulfoxide), and 962 cm^{-1} (*trans* double bond).

Anal. Calcd for $C_7H_{13}NO_3S$: C, 43.96; H, 6.85; N, 7.32. Found: C, 43.7; H, 6.95; N, 7.20.

Although slightly levorotatory fractions could be isolated from the mother liquor, a pure chromatographically homogeneous (−)-sulfoxide could not be isolated.

Preparation of Mixed Crotyl- and Butenylcysteine Sulfoxides 3 and Cyclization to 4 and 5.—Because of the difficulty of separating mixtures of crotyl- and butenylcysteines, it was advantageous to oxidize the mixture to the sulfoxides and to cyclize the crude product as here described. A suspension of 20 g (0.114 mol) of a mixture of 40% 1-butenyl- and 60% 2-butenyl-L-cysteines in 900 ml of water was oxidized with 16 ml of 30% hydrogen peroxide for 27 hr at 25°. Cyclization of the crude dried product was accomplished in 1000 ml of 2 *N* ammonium hydroxide (7 days at 25°).

Crotylcysteine sulfoxide and other primary amino compounds were removed from the product by reaction with sodium 2,4,6-trinitrobenzene sulfonate as described previously.[4] Salts were removed in the usual manner with Dowex 50 (H^+) and the ammoniacal eluate from the ion exchanger on concentration yielded 2.66 g of **5** (30.6% based on the 1-butenyl content of the starting material). Recrystallization from 50% aqueous ethanol gave pure **3-(*R*)-carboxy-5-(*R*)-ethyl-1,4-thiazine S-(*R*)-oxide (5)** as tiny prisms: dec pt 270°; $[\alpha]^{26}_D$ −66.2° (*c* 2, 2.5 *N* hydrochloric acid), −101.2° (*c* 2, water); ir, strong at 1640 (ionized carboxyl) and at 1022 cm^{-1} (sulfoxide).

Anal. Calcd for $C_7H_{13}NO_3S$: C, 43.96; H, 6.85; N, 7.32. Found: C, 44.0; H, 6.74; N, 7.30.

Compound **5** did not form a crystalline hydrochloride. On paper chromatography the compound moved with an R_f relative to alanine of 0.91, and gave an extremely weak yellow spot with the copper ninhydrin reagent.

The mother liquor after removal of **5** was acidified with hydrochloric acid, taken to dryness *in vacuo*, and crystallized from water–acetone (1:8) to yield 1.36 g of **4** as the hydrochloride (13% based on the original 1-butenylcysteine content). Recrystallization from aqueous acetone yielded pure **3-(*R*)-carboxy-5-(*S*)-ethyl-1,4-thiazane S-(*S*)-oxide hydrochloride (4)**: mp 230–238° dec; ir, strong at 1745 (un-ionized carboxyl) and at 1005, 1024, and 1035 cm^{-1} (sulfoxide region).

Anal. Calcd for $C_7H_{13}NO_3S \cdot HCl$: C, 36.92; H, 6.20; N, 6.15; Cl, 15.57. Found: C, 37.0; H, 6.19; N, 6.16; Cl, 15.6.

The hydrochloride of **4** was converted to the free amino acid which was crystallized from water–acetone (1:10) as large coarse prisms: mp 243–245° dec; $[\alpha]^{25}_D$ −22.7° (*c* 2.5, 3 *N* hydrochloric acid) and −32.5° (*c* 2, water); ir, strong at 1640 (ionized carboxyl) and at 1027 cm^{-1} (sulfoxide).

Anal. Calcd for $C_7H_{13}NO_3S$: C, 43.96; H, 6.85; N, 7.32. Found: C, 43.8; H, 6.95; N, 7.28.

Paper chromatography with the solvent system already described gives an extremely faint yellow spot with copper–ninhydrin reagent; relative R_f with respect to alanine, 1.26.

Cyclization of (±)-*trans*-S-(1-Butenyl)-L-cysteine Sulfoxide

(9) Infrared spectra were determined as potassium bromide disks in a Perkin-Elmer Model 237 spectrophotometer. All nmr spectra were taken on a Varian Associates HR-100 spectrometer to which had been added an internal field-frequency lock built at this laboratory. Paper chromatograms were run on Whatman No. 1 paper with butanol–acetic acid–water (63:10:27) and compounds were detected with the copper–ninhydrin spray reagent of E. D. Moffat and R. I. Lytle [*Anal. Chem.*, **31**, 926 (1959)]. Reference to a company or product name does not imply approval or recommendation of the product by the U. S. Department of Agriculture to the exclusion of others that may be suitable.

(3) to 4 and 5.—A solution of 2.70 g (0.0141 mol) of 3 ($[\alpha]^{25}D$ +5°) in 500 ml of 2 *N* ammonium hydroxide was allowed to stand 5 days at 25° and the products were isolated as before. Yields of 492 mg (18.2%) of isomer 4 and 370 mg (11.5%) of 5 hydrochloride were obtained.

Oxidation of Sulfoxides 4 and 5 to the Corresponding Sulfones 7 and 9.—A solution of 700 mg (0.00366 mol) of 5 in 120 ml of 0.25 *N* sulfuric acid was oxidized with 464 mg of potassium permanganate. After removal of sulfate and manganese dioxide and purification with a cation exchanger, a yield of 312 mg of **3-(*R*)-carboxy-5-(*R*)-ethyl-1,4-thiazane S-dioxide** (9) was obtained, identified by ir and nmr.

Oxidation of a sample of 4 (200 mg) in a similar manner yielded 70 mg of **3-(*R*)-carboxy-5-(*S*)-ethyl-1,4-thiazane S-dioxide** (7), established by ir.

Reduction of Sulfoxide 4 to Sulfide 6.—Hydriodic acid reduction of 1.30 g (0.0057 mol) of 4 HCl gave 902 mg (89%) as the free amino acid. Recrystallization from water–ethanol (1:4) yielded pure **3-(*R*)-carboxy-5-(*S*)-ethyl-1,4-thiazane** (6) as large lathlike crystals: mp 256 dec; ir, no sulfoxide absorption; $[\alpha]^{26}D$ −58.8° (*c* 2, water), $[\alpha]^{25}D$ −33.8° (*c* 2.5, 1 *N* hydrochloric acid).

Anal. Calcd for $C_7H_{13}NO_2S$: C, 47.97; H, 7.48. Found: C, 47.8; H, 7.31.

Reduction of Sulfoxide 5 to Sulfide 8.—A sample of 1.496 g (0.00782 mol) of 5 was reduced and the product was crystallized from water–ethanol (1:5) to yield the sulfide, **3-(*R*)-carboxy-5-(*R*)-ethyl-1,4-thiazane** (8) (77%), as rectangular prisms: mp 275–277° dec (phase change above 230°, prisms → needles); sulfoxide absent by ir; $[\alpha]^{25}D$ −82.5° (*c* 1.8, water), −61.07° (*c* 2.2, in 3 *N* hydrochloric acid).

Anal. Calcd for $C_7H_{13}NO_2S$: C, 47.97; H, 7.48; N, 7.99. Found: C, 48.0; H, 7.45; N, 7.98.

Registry No.—2, 19206-35-0; 3, 19206-36-1; 4, 19206-37-2; 4 HCl, 19206-38-3; 5, 19206-39-4; 6, 19206-40-7; 8, 19206-41-8.

Acknowledgment.—We are grateful to Nancy Bennett for assistance with nmr spectra and to L. M. White and Geraldine Secor for analyses.

The Reductic Acid-^{14}C Derived from D-Xylose-1-^{14}C and 2-Furaldehyde-α-^{14}C[1,2]

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In addition to its formation from hexuronic acids and polyuronides, reductic acid (2,3-dihydroxy-2-cyclopenten-1-one) has been reported to be formed from both D-xylose[3] and its structurally related dehydration product, 2-furaldehyde.[4] Subsequent to these reports, several investigators[5–7] have attempted to explain the mechanism of formation of this compound from both D-xylose and 2-furaldehyde, and, in all cases, these suggestions predict that C-1 of D-xylose and the α-carbon atom of 2-furaldehyde should ultimately reside at C-2 of reductic acid.

TABLE I

% DISTRIBUTION OF ISOTOPE IN REDUCTIC ACID-^{14}C

Source	C-2[a]	C-1 and C-3[b]	C-4 and C-5[b]
D-Xylose-1-^{14}C	58.8	41.2	0.3
2-Furaldehyde-α-^{14}C	57.0	42.0	1.0

[a] Determined by difference after conversion of reductic acid-^{14}C into succinic acid-^{14}C. [b] Determined by difference after the conversion of succinic acid-^{14}C into ethylene diamine *via* a Curtius degradation.

In this work, some yield figures and structural relationships between reactants and product were determined using D-xylose-1-^{14}C and 2-furaldehyde-α-^{14}C as starting materials in the conversion. The former compound was obtained commercially and the latter was prepared from D-xylose-1-^{14}C, a conversion which is known[8] to give 2-furaldehyde exclusively labeled at the α-carbon atom. These compounds were converted into reductic acid at 150° in 5% sulfuric acid in low yield (0.24% in the case of D-xylose, calculated from isotope dilution figures). Structural relationships were investigated by systematic degradation of the reductic acid-^{14}C obtained from these precursors. Conversion of reductic acid into succinic acid allowed a determination of the radiochemical activity present at C-2 of reductic acid and since, in the reductic acid molecule, the oxygen-bearing carbon atoms 1 and 3 are equivalent as are the methylene carbon atoms 4 and 5 and are represented by, respectively, the carboxyl carbon atoms and the methylene carbon atoms of succinic acid, a determination of the specific activity of the ethylene diamine derived from succinic acid of known activity *via* a Curtius degradation allowed the determination of the radiochemical activity residing in both pairs of carbon atoms. Degradation of the reductic acid-^{14}C obtained from either D-xylose-1-^{14}C or 2-furaldehyde-α-^{14}C gave identical results (Table I) with about 60% of the activity at C-2 and 40% at C-1 and C-3. In both cases, negligible activity was found in the methylene carbon atoms 4 and 5.

The identical label distribution in the reductic acid indicates a common primary source and suggests that it is 2-furaldehyde derived, since the latter is readily formed from D-xylose under the conditions of formation of reductic acid. That pentoses are sources of reductic acid has been widely accepted exclusively on the basis of the experimental findings of Reichstein and Oppenauer[3] who reported its isolation, in crystalline form, in about 0.5% yield starting from D-xylose.

In a recent study of the formation of reductic acid from D-galacturonic acid,[9] it was found that, in 90% of the reaction product, C-1 of the uronic acid corresponded to C-2 of reductic acid, indicating that this fraction of the product arose in a manner consistent with mechanism proposals on this subject.[5–7] In 10% of the product, however, C-1 of the uronic acid was found at C-1–C-3 of reductic acid and represented an un-

(1) Presented at the 156th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1968.

(2) Journal Paper No. 5506, Missouri Agricultural Experiment Station.

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