

Isomeric 3-Carboxy-1,4-thiazane S-Oxides

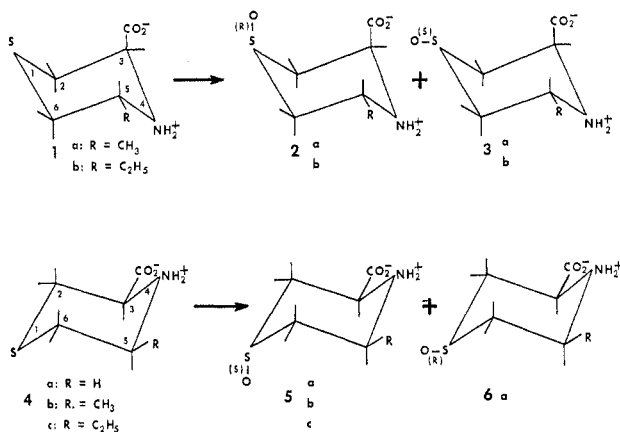
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3-(*R*)-Carboxy-5-(*R*)-methyl-1,4-thiazane S-(*S*)-oxide (**3a**) and the ethyl homolog **3b**, isomers of the corresponding *R* sulfoxides **2a** and **2b**, have been prepared. An isomer of chondrine (**5a**) with the sulfoxide in the opposite configuration (**6a**) has also been obtained. Nmr and infrared spectra of the new isomers are generally consistent with conformations with sulfoxide equatorial, but abnormally high *gauche* coupling constants for **3a** and **3b** (equatorial sulfoxides) suggest a probable highly puckered chair form for these compounds.

In previous investigations, the 3-carboxy-1,4-thiazane S-oxides (axial) (**2a** and **2b**) have been obtained from the cyclization of the corresponding 1-propenyl-² and 1-butenyl-L-cysteine S-oxides.³ Chondrine⁴ (**5a**) was also prepared by oxidation of the corresponding sulfide **4a**. We now report the preparation of the corresponding diastereomers with opposite configuration at sulfoxide **3a**, **3b**, and **6a**. The conformations of the three new sulfoxides were established by nmr.



Reduction of the previously prepared sulfoxide **2a** (R = CH₃) to sulfide **1a** and reoxidation yielded a mixture of the original **2a**, [α]_D²⁵ -113° (water), as the less soluble isomer and the new sulfoxide **3a**, [α]_D²⁵ -25.6° (water). Similarly, sulfide **1b** (R = C₂H₅) yielded on oxidation a mixture of **2b**, [α]_D²⁷ -101° (water), as the less soluble isomer and the new isomer **3b**, [α]_D²⁷ -28.7° (water). Reduced chondrine **4a** (R = H) on oxidation yielded chondrine (**5a**), [α]_D²⁵ +20.0° (water), and the new isomer **6a**, [α]_D²⁵ -55.1° (water).

The conformations of asymmetric centers and the conformation in the solid state of **5b** (cycloalliin)⁵ and of **2a**⁶ are known from X-ray analysis. The configurations of all asymmetric centers of the corresponding ethyl homologs **5c** and **2b** have been established by optical rotation and chemical correlation with **5b** and **2a**.³

The conformation of chondrine (**5a**) has recently been established from X-ray analysis.⁶ The new sulfoxides **3a** and **3b** are *S* therefore at sulfoxide and the isomer **6a** of chondrine is *R* at this center. Since many cyclic sulfoxides have been shown to be thermodynamically

more stable in the axial than in the equatorial conformation,^{7,8} it was necessary to establish the conformations of the new isomers.

Table I gives nmr data for the pairs of isomers **2a** and **3a**, **2b** and **3b**, and **5a** and **6a** and also for cycloalliin (**5b**) (R = CH₃) and its ethyl homolog **5c** (R = ethyl). Figures 1 and 2 show the nmr spectra of **2a** and **3a**. The spectra were measured at 100 MHz in D₂O-*t* BuOH (internal standard) and because of the unusual values for some of the coupling constants, ABX calculations to improve the parameters were applied wherever possible. The accuracy of the values for the coupling constants for the six ring protons in the most critical case **3a** may be judged by calculations of parameter ratios and comparison with previously published data.⁹

The coupling constants of the ring protons of **3a** calculated from two ABX systems are $J_{5,6} = 3.1$ (*ae*) and 8.6 Hz (*aa*), $J_{6,6'} = 13.5$ Hz (*gem*), $J_{2,3} = 3.4$ (*ae*) and 7.4 Hz (*ee*), and $J_{2,2'} = 13.9$ Hz (*gem*). These values, although anomalous, are more consistent with a conformation with the sulfoxide equatorial, as shown in **3a**, than with the inverted chair conformation: $J_{5,6} = 8.6$ Hz (*aa*) is rather small and $J_{2,3} = 7.4$ Hz (*ee*) is abnormally large when compared with the corresponding coupling constants of the isomeric axial sulfoxide **2a**. On the other hand, inversion of the ring of **3a** to the opposite chair conformation with sulfoxide and methyl both axial and carboxyl equatorial would yield far more improbable assignments, $J_{2,3} = 3.4$ (*aa*) and 7.4 Hz (*ae*), to be compared with cycloalliin (**5b**), differing only in the configuration of C₅ with $J_{2,3} = 12.9$ (*aa*) and 2.8 Hz (*ae*). The unusually large effect of the equatorial sulfoxide on the coupling constants of the 2 and 3 protons may be rationalized by assuming a highly puckered chair form. The possibility that in solution two opposite interconvertible chair forms exist in equilibrium seems unlikely, since the coupling constants do not change significantly with temperature. Thus $J_{2,3}$ (*ee*) has the values 7.4, 7.6, and 7.6 Hz in D₂O at 31, 70, and 95°, respectively. Compound **3b** similarly

(7) J. C. Martin and J. J. Uebel, *J. Amer. Chem. Soc.*, **86**, 2936 (1964).(8) C. R. Johnson and D. McCants, Jr., *ibid.*, **87**, 1109 (1965).(9) The criteria for the validity of the ABX approximation of an ABC system follow: I ($\nu_C - \nu_A$) + $\frac{1}{2}(\mp J_{AB} \pm J_{BC}) \gg J_{AB}/2$; II ($\nu_C - \nu_B$) + $\frac{1}{2}(\pm J_{AB} \pm J_{AC}) \gg J_{BC}/2$.Calculation of the ratios of left side to right side of the inequalities gives for the 2,3 protons of **3a** for I, 70.5 and 74.4, and for II, 21.2 and 24.1. For the 5,6 protons, the ratios are I, 21.0 and 23.4, and II, 37.3 and 40.4.These are to be compared with nmr analysis of C. A. Reilly and J. D. Swalen [*J. Chem. Phys.*, **32**, 1378 (1960)] of styrene epoxide. An ABX analysis of the spectrum gave $J_{AB} = 5.66$, $J_{AC} = 2.42$, and $J_{BC} = 4.10$ Hz. An iterative computer procedure changed these constants only slightly to $J_{AB} = 5.65$, $J_{AC} = 2.49$, and $J_{BC} = 4.04$ Hz. The corresponding parameter ratios in the latter case, however, were smaller than ours for the 2,3 protons of **3a**, namely I, 34.4 and 36.1, and II, 15.0 and 16.6.

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

(2) J. F. Carson and L. E. Boggs, *J. Org. Chem.*, **31**, 2862 (1966).(3) J. F. Carson, R. E. Lundin, and L. M. Boggs, *ibid.*, **34**, 1996 (1969).(4) J. F. Carson and F. F. Wong, *ibid.*, **29**, 2203 (1964).(5) K. J. Palmer and K. S. Lee, *Acta Crystallogr.*, **20**, 790 (1966).

(6) K. J. Palmer and K. S. Lee, unpublished data.

TABLE I
 NMR SPECTRAL DATA^a FOR 3-CARBOXY-1,4-THIAZANE S-OXIDES IN D₂O-*t*-BuOH AT 31°

Compd		H-6 (a)	H-6 (e)	H-5	H-2 (a)	H-2 (e)	H-3
2a R = CH ₃ Ax S-O	δ^b J^d	q, 1.82 $J_{6,6'} = 15.0$ (gem) $J_{5,6} = 10.8$ (aa)	d of t, 2.06 $J_{6,6'} = 14.0$ (gem) $J_{5,6} = 2.6$ (ae) $J_{2,6} = 2.6$ (lr)	m, 3.20	$q,^c$ 2.00 $J_{2,2'} = 15.3$ (gem) $J_{2,3} = 5.3$ (ae)	d ^c of q, 2.50 $J_{2,2'} = 15.3$ (gem) $J_{2,3} = 3.8$ (ee) $J_{2,6} = 2.1$ (lr)	t, 3.06 $J_{2,3} = 3.8$ (ee) $J_{2,3} = 5.3$ (ae)
3a R = CH ₃ Eq S-O	δ' J	$q,^c$ 1.83 $J_{6,6'} = 13.5$ (gem) $J_{5,6} = 8.6$ (aa)	q^c and d, 2.19 $J_{6,6'} = 13.5$ (gem) $J_{5,6} = 3.1$ (ae) $J_{6,2} = 2.0$ (lr)	$m,^c$ 2.79 $J_{5,6} = 8.6$ (aa) $J_{5,6} = 3.1$ (ae) $J_{5, \text{CH}_3} = 7.0$	$q,^c$ 2.08 $J_{2,2'} = 13.9$ (gem) $J_{2,3} = 3.4$ (ae)	q^c of d, 2.46 $J_{2,2'} = 13.9$ (gem) $J_{2,3} = 7.4$ (ee) $J_{2,6} = 2.0$ (lr)	$q,^c$ 3.30 $J_{2,3} = 7.4$ (ee) $J_{2,3} = 3.4$ (ae)
2b R = C ₂ H ₅ Ax S-O	δ' J	q, 1.82 $J_{6,6'} = 15.5$ (gem) $J_{5,6} = 11.5$ (aa)	d of t, 2.13 $J_{6,6'} = 15.0$ (gem) $J_{5,6} = 2.5$ (ae) $J_{2,6} = 2.5$ (lr)	m, 3.10	$q,^c$ 2.03 $J_{2,2'} = 15.3$ (gem) $J_{2,3} = 5.8$ (ae)	d ^c of q, 2.56 $J_{2,2'} = 15.3$ (gem) $J_{2,3} = 4.2$ (ee) $J_{2,6} = 2.5$ (lr)	$q,^c$ 3.06 $J_{2,3} = 4.2$ (ee) $J_{2,3} = 5.8$ (ae)
3b R = C ₂ H ₅ Eq S-O	δ' J	$q,^c$ 1.81 $J_{6,6'} = 13.8$ (gem) $J_{5,6} = 9.6$ (aa)	d ^c of q, 2.30 $J_{6,6'} = 13.8$ (gem) $J_{5,6} = 2.9$ (ae) $J_{6,2} = 2.0$ (lr)	$m,^c$ 2.56 $J_{5,6} = 9.6$ (aa) $J_{5,6} = 2.9$ (ae)	$q,^c$ 2.09 $J_{2,2'} = 13.5$ (gem) $J_{2,3} = 3.9$ (ae)	$q,^c$ 2.48 $J_{2,2'} = 13.5$ (gem) $J_{2,3} = 6.9$ (ee) $J_{2,6} =$ (ur)	$q,^c$ 3.28 $J_{2,3} = 6.9$ (ee) $J_{2,3} = 3.9$ (ae)
5b R = CH ₃ Ax S-O	δ' J	$q,^c$ 1.63 $J_{6,6'} = 15.3$ (gem) $J_{5,6} = 12.5$ (aa)	d ^c of t, 2.10 $J_{6,6'} = 15.3$ (gem) $J_{5,6} = 2.4$ (ae) $J_{6,2} = 2.7$ (lr)	$m,^c$ 2.79 $J_{5,6} = 12.5$ (aa) $J_{5,6} = 2.4$ (ae) $J_{5, \text{CH}_3} = 6.9$	$q,^c$ 1.79 $J_{2,2'} = 14.7$ (gem) $J_{2,3} = 12.9$ (aa)	d ^c of t, 2.37 $J_{2,2'} = 14.7$ (gem) $J_{2,3} = 2.8$ (ae) $J_{2,6} = 2.5$ (lr)	$q,^c$ 3.08 $J_{2,3} = 12.9$ (aa) $J_{2,3} = 2.8$ (ae)
5c R = C ₂ H ₅ Ax S-O	δ' J	q, 1.57 $J_{6,6'} = 15.0$ (gem) $J_{5,6} = 12.5$ (aa)	d of t, 2.18 $J_{6,6'} = 15.0$ (gem) $J_{5,6} = 2.7$ (ae) $J_{6,2} = 2.7$ (lr)	m, 2.5-2.7	$q,^c$ 1.81 $J_{2,2'} = 14.6$ (gem) $J_{2,3} = 13.3$ (aa)	d ^c of t, 2.37 $J_{2,2'} = 14.6$ (gem) $J_{2,3} = 2.6$ (ae) $J_{2,6} = 2.7$ (lr)	$q,^c$ 3.08 $J_{2,3} = 13.3$ (aa) $J_{2,3} = 2.6$ (ae)
5a R = H Ax S-O							q, 3.07 $\Sigma J_{2,3} = 15.3$
6a R = H Eq S-O							q, 2.91 $\Sigma J_{2,3} = 13.0$

^a Obtained at 100 MHz. ^b Chemical shifts are in parts per million downfield from *t*-BuOH; d = doublet; d of t = doublet of triplets; d of q = doublet of quartets; t = triplet; q = quartet; m = multiplet; lr = long range, ur = unresolved. ^c Calculated by the ABX approximation. All other parameters are first order. Coupling constants are presented as absolute values. ^d Coupling constants are in hertz.

has a high coupling constant, $J_{2,3}$ (ee) = 6.9 Hz, but the data are again more consistent with a conformation with the sulfoxide equatorial. In the nmr spectra of **5a** and **6a**, only the H-3 resonances could be identified. The outer line spacings of the two quartets, 15.3 and 13.0 Hz, which are equal to $\Sigma J_{2,3}$ in an ABX approximation, require a diaxial relation in each case in agreement with the assigned conformations.

Table II shows the sums $\Sigma J_{2,3}$ and $\Sigma J_{5,6}$ of the ABX

TABLE II

Compd	R	S-O	$\Sigma J_{2,3}$	$\Sigma J_{5,6}$
2a	CH ₃	Ax	9.1 (no diax)	16.6 (diax)
3a	CH ₃	Eq	10.8 (no diax)	11.7 (diax)
2b	C ₂ H ₅	Ax	10.0 (no diax)	14.0 (diax)
3b	C ₂ H ₅	Eq	10.8 (no diax)	12.5 (diax)
5b	CH ₃	Ax	15.7 (diax)	14.9 (diax)
5c	C ₂ H ₅	Ax	15.9 (diax)	15.2 (diax)
5a	H	Ax	15.3 (diax)	
6a	H	Eq	13.0 (diax)	

systems of the eight compounds. In particular, **3a** (R = CH₃, equatorial SO) has $\Sigma J_{2,3} = 10.8$ (diaxial relation absent) and $\Sigma J_{5,6} = 11.7$ Hz (diaxial relation) and **3b** (R = C₂H₅, equatorial SO) has $\Sigma J_{2,3} = 10.8$ (no diaxial relation) and $\Sigma J_{5,6} = 12.5$ Hz (diaxial relation). The near equality of these values suggests the need of caution in using this sum as a criterion of diaxial or nondiaxial relations in the absence of additional information. The nmr spectra show long-range coupling of the order of 2.0-2.7 Hz between the equatorial 2 and 6 protons. This phenomenon has been

observed before, not only with cyclic sulfoxides but with the corresponding sulfides.¹⁰

Physical methods have been developed for distinguishing axial from equatorial sulfoxides, including relative proton chemical shifts and vicinal geminal coupling constants in nmr and shifts in the ir sulfoxide stretching frequencies. It was of interest to determine whether any of these methods would be applicable to a molecule with two heteroatoms further complicated by the presence of two charged groups. In a number of cases, it has been shown that a proton in a *syn* axial position with respect to an axial sulfoxide is more deshielded than a proton in the same position with an equatorial sulfoxide.¹¹ Compound **2a** (axial sulfoxide) has H-5 (*syn*-axial) at δ' 3.20 ppm, and **3a** (equatorial sulfoxide) has H-5 (axial) at δ' 2.79 ppm. Similarly, **2b** (axial sulfoxide) has H-5 (*syn*-axial) at δ' 3.10 ppm, and the isomeric **3b** (equatorial sulfoxide) has δ' 2.56 ppm for H-5. The greater downfield shift of H-5 in the axial sulfoxides than in the corresponding equatorial sulfoxides shows that the *syn*-axial effect applies to these two cases.

Lambert and Keske,¹² in studies of the low-temperature nmr spectra of thiane S-oxides, showed that the difference in chemical shifts of the α geminal protons [Δ_{ae} (α)] was greater for the equatorial sulfoxide

(10) (a) Y. Allingham, R. C. Cookson, and T. A. Crabb, *Tetrahedron*, **24**, 1989 (1968); (b) A. B. Foster, T. D. Inch, M. H. Qadir, and J. M. Webber, *Chem. Commun.*, 1086 (1968).

(11) (a) K. W. Buck, A. B. Foster, W. D. Pardoe, M. H. Qadir, and J. M. Webber, *ibid.*, 759 (1966); (b) A. B. Foster, J. M. Duxbury, T. D. Inch, and J. M. Webber, *ibid.*, 881 (1967).

(12) J. B. Lambert and R. G. Keske, *J. Org. Chem.*, **31**, 3429 (1966).

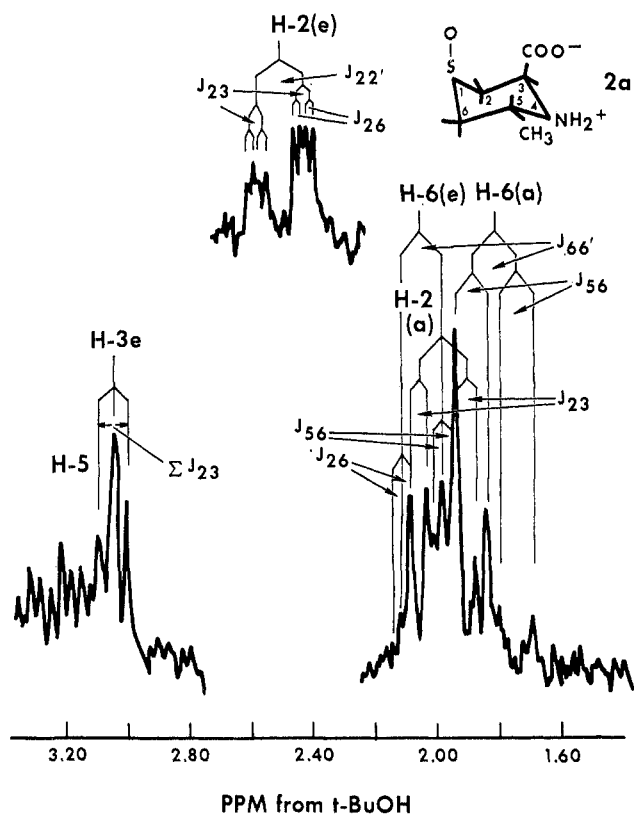


Figure 1.—Partial nmr spectrum of 3-(*R*)-carboxy-5-(*R*)-methyl-1,4-thiazane *S*-(*R*)-oxide in D_2O (*t*-BuON internal standard).

(axial lone pair) (0.87 ppm) than for an axial sulfoxide (equatorial lone pair) (0.48 ppm). For the H-2 geminal protons of the axial sulfoxides **2a** and **2b**, $\Delta a_e = 0.50$ and 0.53 ppm, respectively, while for the corresponding protons of the equatorial sulfoxides **3a** and **3b**, $\Delta a_e = 0.38$ and 0.39 ppm. The geminal shift differences for the 2 protons on the carboxyl side of the ring are small and opposite to the observations of Lambert and Keske for simple 1,4-thiane oxides. On the other hand, for the H-6 geminal protons of **2a** and **2b**, $\Delta a_e = 0.24$ and 0.31 ppm, while for **3a** and **3b** $\Delta a_e = 0.36$ and 0.49 ppm, respectively. The differences are again small but now agree qualitatively with Lambert and Keske's observations.

Lambert and Keske¹² and Foster, *et al.*,^{10b} have observed that vicinal geminal coupling constants for an axial sulfoxide are generally larger in absolute value (larger negative values) than for the corresponding equatorial sulfoxides. Geminal coupling constants shown in Table I are in agreement with this rule. The axial sulfoxides **2a**, **2b**, **5b**, and **5c** have $J_{2,2'}$ and $J_{6,6'}$ in the range 14.5–15.3 Hz. For the equatorial sulfoxides **3a** and **3b**, $J_{2,2'}$ and $J_{6,6'}$ are in the range 13.5–13.9 Hz. The differences are more significant if one compares corresponding J (*gem*) for the isomeric pairs **2a** and **3a** and **2b** and **3b**. For **2a** (axial) $J_{2,2'} = 15.3$ and $J_{6,6'} = 14.5$ Hz. For **3a** (equatorial) $J_{2,2'} = 13.9$ and $J_{6,6'} = 13.5$ Hz. For **2b** (axial) $J_{2,2'} = 15.3$ and $J_{6,6'} = 15.2$ Hz. For **3b** (equatorial) the corresponding values are 13.5 and 13.8 Hz, respectively.

In the infrared, the stretching frequencies for equatorial sulfoxides are generally higher than for axial sulfoxides.¹³ Our sulfoxides are in general agreement

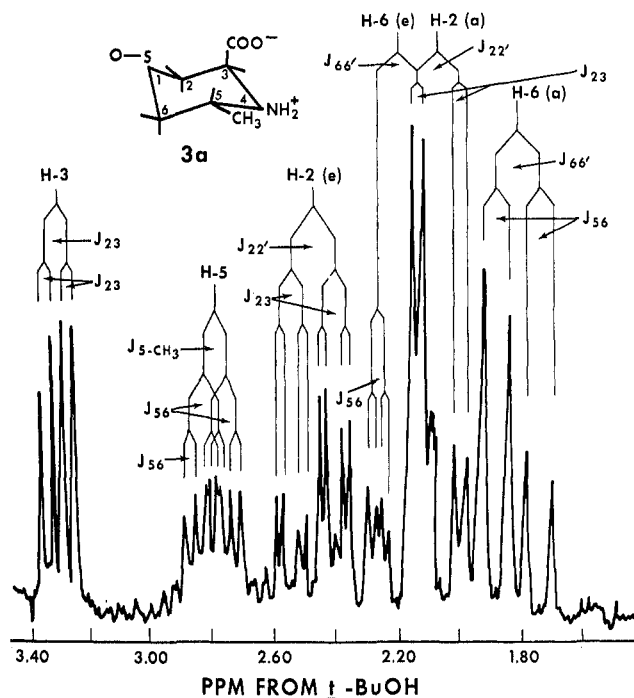


Figure 2.—Partial nmr spectrum of 3-(*R*)-carboxy-5-(*R*)-methyl-1,4-thiazane *S*-(*S*)-oxide in D_2O (*t*-BuOH internal standard).

with this rule. In the ir (KBr disk), **2a** (axial) has bands at 1025 (weak) and 1040 cm^{-1} (strong), while the equatorial isomer **3a** has absorption at 1055 cm^{-1} . For the ethyl homologs, **2b** (axial) has absorption at 1025 cm^{-1} and the corresponding equatorial isomer **3b** has bands at 1050 and 1060 cm^{-1} . Chondrine (**5a**) has two bands, 1030 and 1040 cm^{-1} , while its equatorial isomer **6a** has the S–O stretching frequency at 1055 cm^{-1} . The two axial sulfoxides, cycloalliin (**5b**) and its ethyl homolog **5c**, have sulfoxide absorption at 1035 cm^{-1} .

Johnson and McCants⁸ have observed that in the oxidation of 4-substituted thianes, a preferential formation of axial or equatorial sulfoxide depends on the oxidizing agent. This relationship has been used as supporting evidence for assigning conformations of cyclic sulfoxides.^{11b,13b} In particular, sodium metaperiodate favors the formation of the axial sulfoxide, and hydrogen peroxide in acetic acid tends to yield more equatorial sulfoxide.⁵ With three of our compounds no discrimination could be detected with these reagents. Oxidation of **4b** ($R = CH_3$) and **4c** ($R = C_2H_5$) with either hydrogen peroxide in acetic acid or with aqueous sodium metaperiodate gave exclusively the axial *S* sulfoxides **5b** and **5c**. Compound **4a** ($R = H$) with aqueous sodium metaperiodate yielded 83% axial sulfoxide **5a** and 17% of the equatorial isomer **6a**. This ratio was unchanged when hydrogen peroxide–acetic acid was the oxidant. The sulfides **1a** and **1b**, on oxidation with hydrogen peroxide in acetic acid, each gave approximately equal amounts of equatorial and axial isomers. Apparently, for obscure reasons, the sulfoxides with an equatorial carboxyl are formed predominately as axial isomers, and with an equatorial methyl or ethyl at C-5 (*S*), only axial isomers are formed.

(13) (a) P. B. D. de la Mare, D. J. Millen, J. G. Tillett, and D. Watson, *J. Chem. Soc.*, 1619 (1963); (b) R. Nagarajan, B. H. Chollar, and R. M. Dodson, *Chem. Commun.*, 550 (1967).

However, the sulfoxides with carboxyl axial and with the methyl or ethyl group at C-5 still equatorial but now of *R* configuration are formed, at least with hydrogen peroxide, with no preference for axial or equatorial sulfoxide.

Experimental Section¹⁴

Oxidation of Deoxycycloalliin (4b to 5b) with Hydrogen Peroxide in Acetic Acid.—To a suspension of 3.787 g (0.0192 mol) of 4b hydrochloride in 350 ml of acetic acid there was added 2.30 ml of 32.9% hydrogen peroxide (15% excess) over a period of 6 hr at 13–15°. The suspension was then stirred for 20 hr at 25°. Removal of acetic acid *in vacuo* and fractional crystallization from 3 *N* hydrochloric acid gave three fractions (combined yield 86.3%) of 5b, all with $[\alpha]^{25}_D$ in water varying from –12.0 to –12.2. Data for authentic cycloalliin hydrochloride hydrate follow: $[\alpha]^{25}_D$ –11.7° (water); ir (identical with authentic compound) 1750 (COOH) and 1035 cm⁻¹ (S–O).

Oxidation of 4b as the free amino acid and fractional crystallization of the sulfoxide as the free base also gave fractions with a constant rotation (combined yield 83%).

Oxidation of 4b with Aqueous Sodium Metaperiodate.—To a solution of 4.29 g (0.0217 mol) of 4b hydrochloride in 150 ml of water, adjusted to pH 7 with sodium bicarbonate and cooled to 0°, 50 ml of 0.491 *M* sodium metaperiodate was added in 10-ml portions over a period of 4 hr. The suspension was kept in the refrigerator overnight and excess periodate was destroyed by the addition of 5 ml of dimethyl sulfide followed by stirring for 8 hr at 0°. The mixture was poured through a column of Dowex 50 (H⁺) (400 cm³) and precipitated iodine was removed by washing with ethanol and then water. The product was eluted with 1.5 *N* ammonium hydroxide and fractionally crystallized as the free base from aqueous ethanol. Three fractions were obtained (81%), with $[\alpha]^{25}_D$ (water) varying from –14.3 to –14.7°. For authentic cycloalliin, the $[\alpha]^{25}_D$ value is –14.8° (water).

Attempted epimerization of cycloalliin by the procedure of Barnsley, *et al.*,¹⁵ which was effective for *N*-acetyl-*S*-ethyl-*L*-cysteine sulfoxide, failed. A solution of 1.035 g of cycloalliin in 50 ml of formic acid (88%), after 17 days at 25° and 48 hr at 55°, showed only slight rotational change owing to slight decomposition. The isolated product showed no change in specific rotation. A solution of cycloalliin in 5 *N* hydrochloric acid gradually decomposes at room temperature, but no evidence of racemization at the sulfoxide can be obtained.

Oxidation of 4c to 5c with Hydrogen Peroxide.—A solution of 1.03 g (0.00589 mol) of 4c in 100 ml of acetic acid was oxidized with 0.85 ml of 30% hydrogen peroxide as in the preparation of cycloalliin to yield 791 mg (70%) of 3-(*R*)-carboxy-5-(*S*)-ethyl-1,4-thiazane *S*-(*S*)-oxide (5c), $[\alpha]^{25}_D$ –22.0° (*c* 3, 2.5 *N* hydrochloric acid), identical with the product previously obtained⁸ by cyclization of butenyl cysteine sulfoxide. Fractional crystallization as the free base or as the hydrochloride showed no significant variation in rotation: ir (free base) 1635 cm⁻¹ (COO⁻) and 1030 cm⁻¹ (S–O); ir (hydrochloride) 1740 (COOH) and 1020 and 1035 cm⁻¹ (S–O).

(14) 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. Reference to a company or product name does not imply approval or recommendation by the U. S. Department of Agriculture to the exclusion of others that may be suitable.

(15) E. A. Barnsley, A. E. R. Thomson, and L. Young, *Biochem. J.*, **90**, 588 (1964).

Oxidation of Deoxychondrine (4a) to Chondrine (5a) and Isomer 6a.—A suspension of 3.829 g (0.0260 mol) of 4a in 175 ml of acetic acid was oxidized with 3.4 ml of 33% hydrogen peroxide by the procedure previously described.¹⁶ The yield of crystalline product was 4.10 g (97%), $[\alpha]^{25}_D$ +8.3°. Repeated crystallization from aqueous ethanol yielded 296 mg of chondrine (5a) as prisms, $[\alpha]^{27}_D$ +20.0° (*c* 2.0, water), identical with chondrine previously prepared⁸ by ir and $[\alpha]_D$: ir 1635 and 1675 (COO⁻) and 1030 and 1040 cm⁻¹ (S–O).

From the mother liquor there was obtained, by many recrystallizations from aqueous methanol, 132 mg as needles or blades of 3-(*R*)-carboxy-1,4-thiazane *S*-(*R*)-oxide, $[\alpha]^{27}_D$ –55.1° (*c* 2, water), ir 1610 (COO⁻) and 1055 cm⁻¹ (S–O).

Anal. Calcd for C₈H₉NO₃S: C, 36.81; H, 5.52. Found: C, 36.5; H, 5.64.

The calculated proportion of isomers was 84.4% axial isomer and 15.6% equatorial isomer.

Oxidation of 4a with sodium metaperiodate as described in the preparations of cycloalliin yielded 84% sulfoxide calculated to be 83.2% axial and 16.8% equatorial.

Oxidation of 1a to 2a and 3a.—Oxidation of 1.412 g (0.00876 mol) of 1a with hydrogen peroxide in acetic acid as previously described yielded, on crystallization from water, 583 mg, $[\alpha]^{25}_D$ –106.2° (water). Recrystallization from water yielded 450 mg of pure 3-(*R*)-carboxy-5-(*R*)-methyl-1,4-thiazane *S*-(*R*)-oxide (2a) as prisms, $[\alpha]^{25}_D$ –113° (*c* 0.9, water), identical with the previously prepared compound by $[\alpha]_D$ and ir: 1600 and 1630 (COO⁻) and 1025 and 1040 cm⁻¹ (S–O).

From the mother liquor by recrystallization from aqueous acetone, there was obtained 270 mg (blades) of 3-(*R*)-carboxy-5-(*R*)-methyl-1,4-thiazane *S*-(*S*)-oxide (3a), $[\alpha]^{27}_D$ –25.6° (*c* 2, water), ir 1620 (COO⁻) and 1055 cm⁻¹ (S–O).

Anal. Calcd for C₈H₁₁NSO₃: C, 40.66; H, 6.26. Found: C, 40.6; H, 6.14.

The yield of mixed isomers was 1.357 g (87.5%), calculated to contain 48% axial (*R*) sulfoxide and 52% equatorial (*S*) sulfoxide.

Oxidation of 1b to 2b and 3b.—A solution of 1.578 g (0.00902 mol) of 1b in 130 ml of acetic acid and 20 ml of water was oxidized with hydrogen peroxide as already described to yield 1.54 g of mixed sulfoxides (89.3%). Crystallization from water yielded 666 mg of 2b, and recrystallization of this fraction yielded 590 mg (prisms) of 3-(*R*)-carboxy-5-(*R*)-ethyl-1,4-thiazane *S*-(*R*)-oxide (2b), $[\alpha]^{27}_D$ –100.9° (*c* 1.1, water), identical by $[\alpha]_D$ and ir with the previously prepared sulfoxide, 2b: ir 1645 (COO⁻) and 1025 cm⁻¹ (S–O).

The more soluble fractions from the mother liquor were recrystallized from aqueous ethanol to yield 290 mg of 3-(*R*)-carboxy-5-(*R*)-ethyl-1,4-thiazane *S*-(*S*)-oxide (3b), $[\alpha]^{25}_D$ –24.7° (*c* 2, water), ir 1600 (COO⁻) and 1050 and 1060 cm⁻¹ (S–O).

Anal. Calcd for C₇H₁₃NO₃: C, 43.96; H, 6.85; N, 7.32. Found: C, 44.0; H, 6.74; N, 7.30.

Registry No.—2a, 7762-85-8; 2b, 19206-39-4; 3a, 23652-72-4; 3b, 23652-73-5; 5a, 23652-74-6; 5b, 23652-75-7; 5c, 19206-37-2; 6a, 23652-77-9.

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(16) Reference 4 contains an error in the Experimental Section, p 2205. Under the heading "(+)-*L*-1,4-Thiazane-3-carboxylic acid 1-Oxide (Chondrine, IV)," the quantity 1.2 ml of 30% hydrogen peroxide should be 2.1 ml of 30% hydrogen peroxide.