solution was concentrated under reduced pressure to a volume of around 20 ml. The suspended acid was recovered by filtration, washed with water, and dried *in vacuo* over anhydrous calcium chloride to give a white powder weighing 344 mg.

The crude acid was suspended in warm aqueous ethanol, and sufficient aqueous sodium hydroxide was added to provide a pH of around 7 at a point where all the acid had dissolved. Additional ethanol was added, and the solution was filtered and concentrated by warming to a volume slightly greater than that which would induce spontaneous crystallization. The sodium salt (III) was recovered as two crops of needles. These were washed with ethanol, and recrystallized from aqueous ethanol to yield a total of 298 mg (83%) of colorless needles: mp 286–287° dec; ν_{max} 3650–3100 (hydroxyl), 1610 cm^{-1} (carboxylate).

Anal. Calcd for $C_{33}H_{53}O_7Na$: C, 67.78; H, 9.14. Found: C, 67.62; H, 9.11.

A 20-mg sample of sodium cholest-5-en-3β-yl-β-D-glucopyranosiduronate (III) in 250 ml of dilute acetate buffer (pH 5, containing 10% ethanol) was incubated for 72 hr at 38° with 100,000 units of β-glucuronidase derived from beef liver. Extraction with chloroform, followed by two crystallizations of the recovered free sterol from ether–methanol, gave 3.2 mg of plates, mp 149–150°. The melting point was unchanged on admixture with an authentic preparation of cholesterol, and the ir spectra of the recovered and reference sterols were identical.

Preparation of Cholest-5-en-3β-yl-β-D-glucopyranosiduronic Acid (II).—Solution of a sample of the twice-crystallized sodium salt (III) in aqueous ethanol, followed by acidification and concentration under reduced pressure, provided a suspension of acid II. The product was recovered by filtration, washed with water, and dried *in vacuo* over anhydrous calcium chloride: mp 232–233° dec; ν_{max} 3600–3100 (hydroxyl), 1735 cm^{-1} (carboxyl).

Anal. Calcd for $C_{33}H_{54}O_7$: C, 70.43; H, 9.67; COOH, 7.99. Found: C, 70.19; H, 9.63; COOH, 7.84.

A sample of purified acid II in tetrahydrofuran was treated with excess ethereal diazomethane. Acetylation of the dried residue or of the crystallized methyl ester (needles, from aqueous tetrahydrofuran) gave, from ethyl acetate–methanol, needles melting at 164–165°. The melting point was unchanged on admixture with an authentic sample of methyl [cholest-5-en-3β-yl 2′,3′,4′-tri-*O*-acetyl-β-D-glucopyranosid]uronate (I), and their ir spectra were identical.

Methyl [5α-Cholestan-3β-yl-2′,3′,4′-tri-*O*-acetyl-β-D-glucopyranosid]uronate (IV) from I.—A solution of 500 mg of methyl [cholest-5-en-3β-yl-2′,3′,4′-tri-*O*-acetyl-β-D-glucopyranosid]uronate (I) in 25 ml of ethyl acetate was shaken for 3 hr in a hydrogen atmosphere in the presence of a 5% palladium-on-carbon catalyst (Engelhard Industries). After removal of the catalyst by filtration and the solvent by evaporation in a stream of nitrogen, the residue was crystallized from ethyl acetate–methanol to furnish 427 mg of needles: mp 180–181°; $[\alpha]_D$ −5°; ν_{max} 1755 (acetate), 1470, 1440, 1370, 1250–1210 cm^{-1} (acetate).

Anal. Calcd for $C_{40}H_{64}O_{10}$: C, 68.15; H, 9.15; CH_3CO, 18.32; OCH_3, 4.40. Found: C, 68.18; H, 9.14; CH_3CO, 18.07; OCH_3, 4.42.

Saponification of 212 mg (0.3 mmol) of methyl [5α-cholestan-3β-yl-2′,3′,4′-tri-*O*-acetyl-β-D-glucopyranosid]uronate (IV), as in the preparation of III from I, gave 148 mg of **sodium 5α-cholestan-3β-yl-β-D-glucopyranosiduronate** as needles from aqueous ethanol: mp 286–287° dec; ν_{max} 3650–3100 (hydroxyl), 1610 cm^{-1} (carboxylate).

Anal. Calcd for $C_{33}H_{55}O_7Na$: C, 67.55; H, 9.45. Found: C, 67.40; H, 9.51.

Incubation of a 20-mg sample of sodium 5α-cholestan-3β-yl-β-D-glucopyranosiduronate with β-glucuronidase, as in the previous example, gave 5.0 mg of leaflets from methanol, mp 141–142°. The melting point was unchanged on admixture with an authentic preparation of cholestanol, and the ir spectra of the isolated and reference sterols were identical.[13]

(13) The object of these hydrolyses was to obtain samples of the free sterols for formal identification, but it was apparent from the low recovery of the sterols that both sterol glucuronides are resistant to hydrolysis by β-glucuronidase of hepatic origin. It was reported earlier [K. D. Voigt, M. Lemmer, and J. Tamm, *Biochem. Z.*, **332**, 550 (1960)] that a preparation of cholesterol β-D-glucuronide (supplied by Professor Rudolph Tscheche but not described in the literature) was not hydrolyzed by the same enzyme preparation. The low rate of hydrolysis of cholesterol β-D-glucuronide by β-glucuronidase of limpet origin is evident from the data of Nagayama, *et al.*,[12] who did not, however, comment on the point.

5α-Cholestan-3β-yl-2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranoside (V) from IV.—To a solution of 200 mg of methyl [5α-cholestan-3β-yl-2′,3′,4′-tri-*O*-acetyl-β-D-glucopyranosid]uronate (IV) in 25 ml of dry ether, 300 mg of lithium aluminum hydride was added. After refluxing for 3 hr, excess reagent was decomposed by the successive addition of ethyl acetate and water. The solution was further diluted with ethyl acetate, washed with acidic and neutral brine, dried with anhydrous sodium sulfate, and evaporated to dryness under reduced pressure. Following reacetylation, the product was crystallized from ethanol, furnishing 95 mg of needles: mp 174.5–175.5°; $[\alpha]_D$ +3°; ν_{max} 1750 (acetate), 1468, 1440, 1365, 1250–1210 cm^{-1} (acetate) [lit. for 5α-cholestan-3β-yl-2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranoside (V) mp 175°; $[\alpha]_D$ +5° ($CHCl_3$)[6]].

Anal. Calcd for $C_{41}H_{66}O_{10}$: C, 68.49; H, 9.25; CH_3CO, 23.95. Found: C, 68.40; H, 9.23; CH_3CO, 23.07.

Registry No.—II, 17435-78-8; III, 19459-08-6; IV, 19459-09-7; V, 19459-10-0; sodium 5α-cholestan-3β-yl-β-D-glucopyranosiduronate, 19459-11-1.

Acknowledgments.—The two-stage methanolysis–saponification of the triacetyl methyl ester (I) to the sodium salt (III) is based on a technique devised earlier by Dr. Vernon Mattox for similar derivatives. We wish to thank him for offering the method to us prior to its publication. We express also our gratitude to our associate, Dr. Marvin Lewbart, who pointed out the feasibility of reducing the saturated triacetyl methyl ester (IV) to the tetraacetyl glucoside (V) with lithium aluminum hydride. The nuclear magnetic resonance spectra were obtained with instruments in the laboratories of Varian Associates whom we wish to thank for this courtesy.

A New Dimer of Pyridoxol (Vitamin B_6)

E. E. HARRIS, J. L. ZABRISKIE, E. M. CHAMBERLIN, J. P. CRANE, E. R. PETERSON, AND W. REUTER

Merck Sharp and Dohme Research Laboratories, Rahway, New Jersey 07065

Received October 3, 1968

A number of syntheses of pyridoxol (**5**) by Diels–Alder condensations of a variety of dienophiles with 5-ethoxy-4-methyloxazole (**1**) have been described.[1] While examining the conversion of adduct **3** of this oxazole and *cis*-1,4-diacetoxybutene-2 (**2**) to pyridoxol in moist acetic acid solvent (Scheme I), we have observed that a high yield of product is obtained from dilute solutions of adduct, but that the yield falls off rapidly as the initial concentration of adduct is increased. However, the apparent yield when measured by the intensity of the pyridoxol chromophore in the total reaction mixture appears essentially independent of concentration (Table I). The bulk of this difference can be accounted for by the presence of a new dimer **6**, N-(5-desoxypyridoxolyl)pyridoxol, isolated from the reaction mixture by ion-exchange chromatography.

(1) E. E. Harris, R. A. Firestone, K. Pfister, 3rd, R. R. Boettcher, F. J. Cross, R. B. Currie, M. Monaco, E. R. Peterson, and W. Reuter, *J. Org. Chem.*, **27**, 2705 (1962); W. Kimel and W. Leimgruber, U. S. Patent 3,250,778 (1966); T. Naito and T. Yoshikawa, *Chem. Pharm. Bull.* (Tokyo), **14**, 918 (1966); R. A. Firestone, E. E. Harris, and W. Reuter, *Tetrahedron*, **23**, 943 (1967).

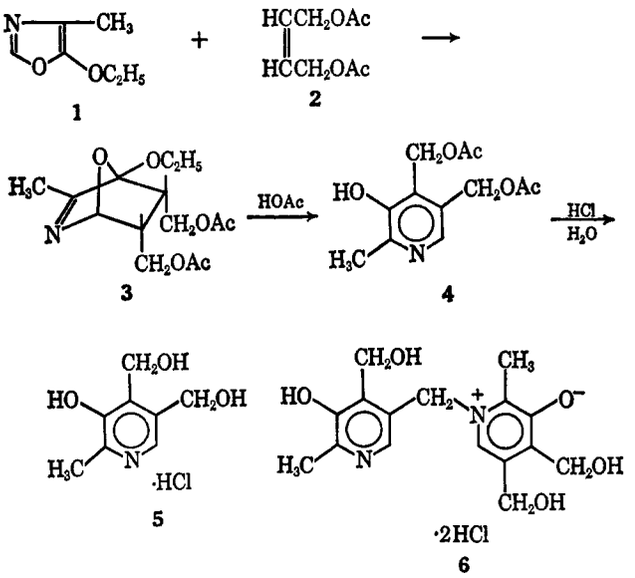
TABLE I

YIELDS OF PYRIDOXOL

[3], M^a	Apparent yield,[b] %	True yield,[c] %
0.019	100	89
0.093	91	75
0.465	93	53
0.930	92	30

[a] Initial concentration in acetic acid. [b] Per cent of theory by uv absorbance of the crude reaction mixture at 292 nm in 0.1 *N* HCl. [c] By quantitative paper chromatography.

SCHEME I



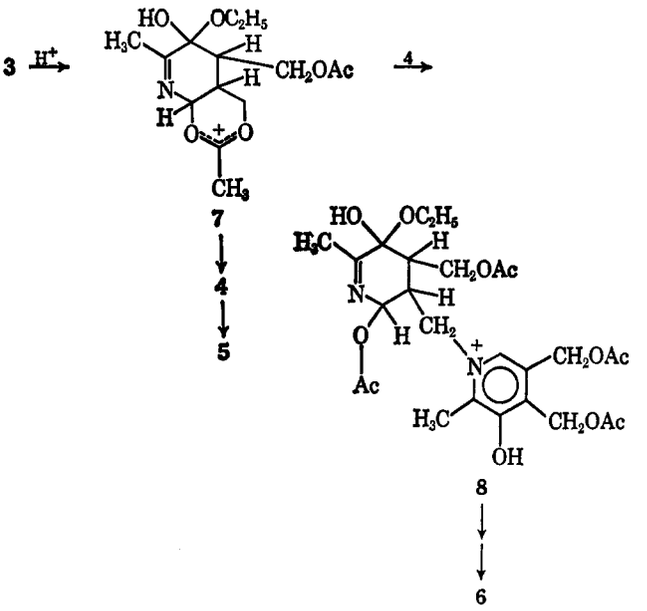
The structure of the dimer **6** was established by elemental analysis of its dihydrochloride, mp 194–197°, which corresponds to the empirical formula $C_{16}H_{20}N_2O_5 \cdot 2HCl$, by its equivalent weight, by a positive Gibbs test indicative of an unsubstituted position *para* to a phenolic hydroxyl,[2] and by its nmr and ultraviolet spectra.

The 60-Mc nmr spectrum of the dimer in D_2O–DCl (Table II) resembles the sum of two nearly equivalent pyridoxol-like molecules,[3] except for the deshielding by 70 cps of one pair of C-5 methylene protons by the quaternary nitrogen and a 40-cps upfield shift of one aromatic proton. In 1 *N* NaOD in D_2O the spectrum exhibits in one of the two methyl groups the exchange of protons typical of quaternized pyridoxine derivatives,[4] while that of the methiodide of **6** shows this exchange in both of the C-2 methyl groups under these conditions.

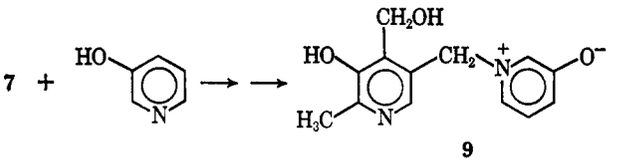
The ultraviolet absorption spectrum of **6** (Table III) at pH 7 shows in phosphate buffer the twin maxima in the 255- and 325-nm region characteristic of pyridoxine derivatives and exhibits in borate buffer the single peak near 295 nm expected only[5] for those derivatives which contain both the free 3-hydroxyl and the free 4-hydroxymethylene functions which permit formation of a cyclic borate ester. These positions are free in both segments of the dimer and no absorbance maxima are observed near 255 and 325 nm.

Pyridoxol diacetate (**4**) alone does not dimerize in the reaction medium. A rational pathway to the dimer must involve the adduct and might well proceed by way of the carboxonium ion **7** which, in addition to the expected aromatization to **4**, would be susceptible to nucleophilic attack at the incipient C-5 methylene carbon[6] by previously formed **4** to yield **8** and ultimately **6** by aromatization through loss of the elements of acetic acid and ethanol and subsequent hydrolysis (Scheme II). High initial concentrations of **3** afford greater concentrations of **4** during the later stages of the reaction, which would increasingly favor dimer formation, as is observed. Clearly nucleophiles other than **4** should attack **7** in this same manner, and indeed

SCHEME II



when the adduct was treated with acetic acid in the presence of added 3-hydroxypyridine a high yield of the analogous mixed product **9** was obtained. The



structural assignment is supported by its elemental analysis, nmr spectrum (Table II), and ultraviolet spectrum (Table III), which shows in borate buffer the presence of both the complexed 292-nm peak and the pair at 248 and 322 nm derived from the 3-hydroxypyridine moiety.

A different dimer of pyridoxol has been isolated from autoclaved solutions of pyridoxol free base by Harris.[7] Because it formed only a monomethiodide, he assigned to it the structure **10**, differing from **6** only by the presence of a C-4 rather than a C-5 methylene linkage to the quaternary nitrogen; more recently Hüttenrauch

(2) H. D. Gibbs, *J. Biol. Chem.* **72**, 649 (1927); E. T. Stiller, J. C. Keresztesy, and J. R. Stevens, *J. Amer. Chem. Soc.*, **61**, 1237 (1939).

(3) W. Korytnyk and B. Paul, *J. Heterocycl. Chem.*, **2**, 481 (1965).

(4) W. Korytnyk and R. P. Singh, *J. Amer. Chem. Soc.*, **85**, 2813 (1963).

(5) J. V. Scudi, W. A. Bastedo, and T. J. Webb, *J. Biol. Chem.*, **136**, 399 (1940).

(6) L. J. Dolby, C. N. Lieske, D. R. Rosencrantz, and M. J. Schwarz, *J. Amer. Chem. Soc.*, **85**, 47 (1963); L. J. Dolby and M. J. Schwarz, *J. Org. Chem.*, **30**, 3581 (1965); O. K. J. Kovács, Gy. Schneider, L. K. Láng, and J. Apjok, *Tetrahedron*, **23**, 4181 (1967); R. J. Oullette and R. D. Robins, *Tetrahedron Lett.* 397 (1968).

(7) S. A. Harris, *J. Amer. Chem. Soc.*, **63**, 3363 (1941).

TABLE II

60-MC NMR SPECTRA[a]

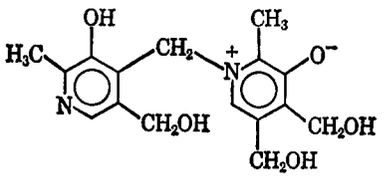
Compd	Solvent	2-Methyl	4-Methylene	5-Methylene	6-H	DOH	Other
Pyridoxol·HCl	D_2O–DCl	163 (3)	307[b] (2)	294[b] (2)	497 (1)	346	
Dimer **6**·2HCl	D_2O–DCl	160 (3)	307 (2)	291 (2)	457 (1)	348	
		164 (3)	309 (2)	364 (2)	502 (1)		
Dimer **6**	D_2O–1 *N* NaOD	140 (3)		292 (2, estd)	457 (1)	284	
		150[c] (3)	*d*	336 (2)	412 (1)		
Dimer **6** methiodide	D_2O	162 (3)	304 (2)	292 (2)	462 (1)	280	
		164 (3)	308 (2)	364 (2)	500 (1)		252[e] (3)
Dimer **6** methiodide	D_2O–1 *N* NaOD	148[c]		292	406	284	238[e]
		152[c]	*d*	348	464		
Compound **9**	D_2O–DCl	167 (3)	302 (2)	369 (2)	497 (1)		Multiplet at 513(2) Multiplet at 482 (2)
Dimer **11**	D_2O–DCl	161 (6)	302 (2)	284 (2)	504 (1)		
			310 (2)	292 (2)			
Dimer **11**	D_2O–1 *N* NaOD	134[f] (3)		241 (2)	457 (1)	292	
		139[f] (3)	*d*	279 (2)			

[a] Data are cps downfield from DSS internal standard. Figures in parentheses are number of protons by integration. [b] Assigned by Korytnyk and Paul. [c] Exchanged rapidly. [d] Masked by DOH. [e] Quaternary methyl. [f] Did not exchange.

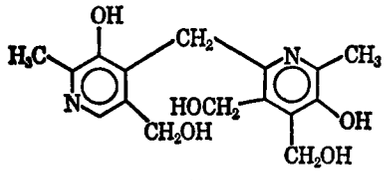
TABLE III

ULTRAVIOLET ABSORPTION SPECTRA IN AQUEOUS SYSTEMS

Compd	Solvent	λ_{max}, nm	$E^{1\%}_{1cm}$
Pyridoxol·HCl	0.1 *N* HCl	292	425
	pH 7 phosphate buffer	324, 254	345, 182
	pH 7 borate buffer	292	300
Dimer **6**·2HCl	0.1 *N* HCl	296	466
	pH 7 phosphate buffer	332, 258	286, 209
	pH 7 borate buffer	296	293
4-Methyl ether of pyridoxol·HCl	pH 7 borate buffer	327, 253	344, 177
Compound **9** free base	pH 7 borate buffer	248, 292, 322	328, 190, 284



10



11

and Zahn[8] have interpreted its relatively facile oxidation by triphenyltetrazolium chloride as support for this N-alkylpyridinium-4-carbinol structure. However, the nmr spectra (Table II) indicate the presence of only one aromatic proton and the absence of a quaternary linkage, since the methyl protons did not exchange in base. In consequence, this dimer is better formulated as Harris' alternative, but less favored, structure **11**.

Experimental Section[9]

Diels–Alder Adduct 3.—A mixture of 127 g (1.0 mol) of 5-ethoxy-4-methyloxazole,[1] 516 g (3.0 mol) of *cis*-1,4-diacetoxybutene-2,[10] and 15 g of powdered calcium oxide was stirred under nitrogen for 30 hr at 115°. The reaction mixture, which contained 30% of unreacted oxazole by glpc (20% DC-200 on Chromasorb W), was filtered and stripped free of oxazole and diacetoxybutene at 0.5-mm pressure, and the residual crude adduct, obtained in almost quantitative yield based on oxazole consumed, was doubly distilled at 0.1 mm and 100° in a falling-film molecular still: no ultraviolet absorbance; nmr ($CDCl_3$) downfield from TMS, 78 (t, CH_3CH_2), 124 cps (s, $2CH_3CO$), 129 cps (s, $CH_3C{=}N$), envelope 148–288 cps (8 protons), 339 cps (d, bridgehead **H**).

Anal. Calcd for $C_{14}H_{21}NO_6$: C, 56.17; H, 7.07; N, 4.68. Found: C, 55.69; H, 6.67; N, 4.91.

Pyridoxol Hydrochloride (5).—Ten grams (0.0334 mol) of crude adduct **3** in 1670 ml of acetic acid 0.4 *M* in water was heated at 50° for 2 hr, freed of acetic acid under reduced pressure, and heated in 100 ml of 0.45 *N* hydrochloric acid at 95° for 2.5 hr. The apparent yield of product calculated from the ultraviolet absorbance of an aliquot of this solution at 292 nm in 0.1 *N* hydrochloric acid was 100%. The yield of pyridoxol determined by quantitative paper chromatography (Whatman No. 4, wet with pH 7 borate buffer and developed 18 hr with *n*-butyl alcohol saturated with the same buffer, the spot corresponding to pyridoxol eluted with borate buffer and evaluated by ultraviolet absorbance) was 89%. Values at other concentrations were determined in the same manner.

Dimer 6.—Eighty-five grams (0.28 mol) of crude adduct **3** in 280 ml of acetic acid 0.4 *M* in water was heated to 50° for 2 hr. The dark mixture was stripped free of acetic acid *in vacuo* and the residue was heated in 800 ml of 0.475 *N* hydrochloric acid at 95° for 2.5 hr to afford a 30% yield of pyridoxol and 33% of dimer **6** by quantitative paper chromatography. The hydrolysis solution was charged to 500 g of Amberlite IR-120 resin on the hydrogen cycle. The resin was washed with water to remove color bodies and eluted with 12 l. of 2 *N* hydrochloric acid. The first 6 l. afforded upon concentration *in vacuo* 17.5 g (30%) of crystalline pyridoxol hydrochloride identical in all respects with an authentic sample. The remaining 6 l. contained 8.4 g of material with a pyridoxinelike uv absorption which was shown by tlc on silica gel in 1:1 $CHCl_3$–MeOH to be mostly dimer **6**.

(8) R. Hüttenrauch and U. Zahn, *Arch. Pharm.*, **300**, 385 (1967).

(9) Melting points are uncorrected. Microanalyses were run by Mr. R. N. Boos. Nmr spectra were run by Mr. R. C. Zerfing on a Varian A-60A instrument.

(10) W. J. Bailey and R. Barclay, Jr., *J. Org. Chem.*, **21**, 328 (1956).

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

J. F. CARSON, ROBERT E. LUNDIN, AND LOIS E. BOGGS

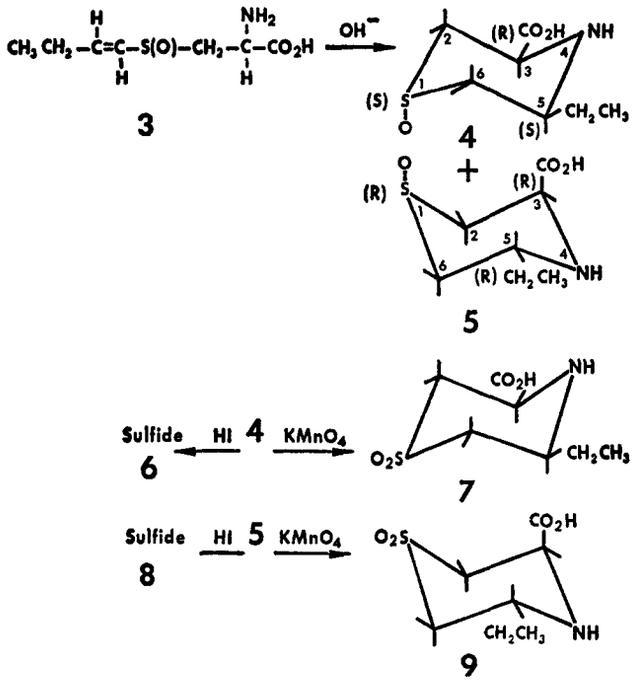
Western Regional Research Laboratory,[1] *Albany, California 94710*

Received September 19, 1968

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.