968 cm.$^{-1}$ but not at 990 and 910 cm.$^{-1}$. Ames and Bowman[16] reported b.p. 87–89° (0.5 mm.), n^{20}D 1.4406 for ethyl *trans*-9-undecenoate. Saponification of the ester furnished 9-undecenoic acid, b.p. 139° (6.5 mm.), n^{26}D 1.4500, in an 88.9% yield based on the starting acid. Iodine value (Wijs): 138.0; calculated for undecenoic acid: 138.4. Infrared spectrum (liquid film) had a distinct absorption at 968 cm.$^{-1}$, not at 990 and 910 cm.$^{-1}$ [reported[16] for *trans*-9-undecenoic acid, b.p. 121–123° (0.7 mm.), n^{20}D 1.4519]. *p*-Phenylphenacyl ester prepared in the usual manner[17] melted at 62.5–63.5° after a single recrystallization from ethanol and gave correct analyses for carbon and hydrogen. Ames and Bowman[16] reported m.p. 64.5–65° for the *p*-phenylphenacyl ester of *cis*-9-undecenoic acid.

7-Keto-16-heptadecenoic Acid.—To a solution of 18.4 g. (0.11 mole) of N-(1-cyclohexenyl)morpholine[18] and 10.9 g. (0.12 mole) of triethylamine in 140 ml. of chloroform was added 20.3 g. (0.1 mole) of 10-undecenoyl chloride[6] in 50 ml. of chloroform over a period of 1 hr. at 35°, and the mixture was maintained at this temperature for an additional 3 hr. The acylated enamine was hydrolyzed in the chloroform solution by refluxing with 50 ml. of 20% hydrochloric acid for 5 hr. and the chloroform layer was separated and washed with water until pH of washing water became 6. The aqueous layer combined with the washings was neutralized to pH 6 with concentrated sodium hydroxide solution and extracted twice with 50-ml. portions of chloroform. The combined chloroform solutions were evaporated to dryness under diminished pressure and the residue was decomposed with 20 g. of potassium hydroxide in 15 ml. of water on a boiling water bath for 10 min. Semisolid material thus obtained was dissolved in 1 l. of hot water and strongly acidified with concentrated hydrochloric acid. The precipitates were collected by filtration, washed with 100 ml. of cold water, and dried. Recrystallizations from *n*-hexane gave the keto acid, m.p. 68.5–69.3°, weighing 27.0 g. (92.7%). ν_{max} (Nujol) at 1710 (broad), 995 and 915 cm.$^{-1}$.

Anal. Calcd. for $C_{17}H_{30}O_3$: C, 72.30; H, 10.71. Found: C, 72.35; H, 10.74.

Semicarbazone prepared by the usual method[19] melted at 110–111.2° after a single recrystallization from ethanol.

Anal. Calcd. for $C_{18}H_{33}O_3N_3$: C, 63.68; H, 9.80. Found: C, 63.65; H, 9.99.

15-Heptadecenoic Acid.—A solution of 14 g. (0.05 mole) of the aforementioned keto acid, 20 ml. of 80% hydrazine hydrate, and 2.8 g. of potassium hydroxide dissolved in 50 ml. of diethylene glycol was heated under reflux for 8 hr. The hot solution was added with 14 g. of potassium hydroxide and 50 ml. of diethylene glycol, and water as well as excess hydrazine hydrate were removed by distillation. The temperature of the content rose gradually up to 185°, when the mixture was heated under reflux for an additional 15 hr. The reaction mass was dissolved in 1.5 l. of water and strongly acidified with concentrated hydrochloric acid. The resulting precipitates were collected after cooling, washed with ice-cold water and dried. Recrystallizations from acetone and *n*-hexane afforded 12.9 g. (86.2%) of colorless leaflets melting at 49.5–50.3°. ν_{max} (Nujol) at 968 cm.$^{-1}$.

Anal. Calcd. for $C_{17}H_{32}O_2$: C, 76.06; H, 12.02. Found: C, 75.89; H, 12.00.

p-Phenylphenacyl ester[17] melted at 86.0–87.0° after two recrystallizations from ethanol.

Anal. Calcd. for $C_{31}H_{42}O_3$: C, 80.47; H, 9.15. Found: C, 80.28; H, 9.01.

Oxidation of 15-Heptadecenoic Acid.—To a solution of 2 g. of the unsaturated acid in 20 ml. of glacial acetic acid was added portionwise 6 g. of chromic acid under vigorous stirring and the mixture was heated under reflux for an additional 1 hr. The reaction mixture was added with 20 ml. of ethanol and evaporated *in vacuo*. The residue was treated with 100 ml. of dilute hydrochloric acid, then with 5% aqueous sodium hydroxide solution, and filtered. When the filtrate was acidified with hydrochloric acid, there separated a white precipitate, which was collected, washed with water, and dried. On recrystallizations from ethyl acetate and glacial acetic acid there was obtained 0.5 g. of tridecane-1,13-dicarboxylic acid, m.p. 112.5–113.5° (reported[3] m.p. 113.5°), which gave correct analyses for carbon and hydrogen.

7-Keto-15-heptadecenoic Acid.—A mixture of 9-undecenoyl chloride[6] and 13.5 g. of N-(1-cyclohexenyl)morpholine was similarly treated as described for 10-undecenoyl chloride, and 17.2 g. of 7-keto-15-heptadecenoic acid, m.p. 70.0–71.5°, was obtained as colorless crystals in a 90% yield after recrystallizations from *n*-hexane. ν_{max} (Nujol) at 970 cm.$^{-1}$. Mixed m.p. with 7-keto-16-heptadecenoic acid was 61.5–64.5°.

Anal. Calcd. for $C_{17}H_{30}O_3$: C, 72.30; H, 10.71. Found: C, 72.17; H, 10.76.

Semicarbazone prepared similarly melted at 111.5–112.8° after recrystallizations from ethanol and showed a marked depression of m.p. when admixed with the semicarbazone of 7-keto-16-heptadecenoic acid.

Anal. Calcd. for $C_{18}H_{33}O_3N_3$: C, 63.68; H, 9.80. Found: C, 63.85; H, 10.01.

The keto acid was reduced in the same manner as described for 7-keto-16-heptadecenoic acid and the unsaturated acid, m.p. 49.5–50.3°, was obtained in an 85.6% yield. Mixed m.p. with the specimen obtained as above showed no depression. The *p*-phenylphenacyl ester of both origin, when admixed, also did not show any depression of melting point.

Reduction of 7-Keto-16-heptadecenoic Acid by the Usual Wolff–Kishner Method.—A mixture of 5.6 g. of the keto acid, 2.8 g. of metallic sodium, and 2.9 g. of hydrazine hydrochloride in 80 ml. of anhydrous ethanol was heated at 185–200° for 96 hr. in a closed vessel as described by Kapp and Knoll[6] and 3.0 g. of unsaturated acid, m.p. 49.0–50.1°, was isolated after several recrystallizations from acetone, petroleum ether (b.p. 40–60°), and aqueous methanol. Mixed m.p. with aforementioned 15-heptadecenoic acid showed no depression. *p*-Phenylphenacyl ester of this unsaturated acid melted at 85.9–87.0° and gave correct analyses for carbon and hydrogen. Mixed m.p. with the ester derived from 15-heptadecenoic acid showed no depression.

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[16] D. E. Ames and R. E. Bowman, *J. Chem. Soc.*, 677 (1952).

[17] R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th ed., John Wiley & Sons, Inc., New York, 1956, p. 200.

[18] S. Hünig, E. Benzing, and E. Lücke, *Ber.*, **90**, 2833 (1957); G. Optiz, H. Hellman, and H. W. Schubert, *Ann.*, **623**, 112 (1959).

[19] Ref. 17, p. 218.

A Seven-Membered Cyclic Ketal of Pyridoxol[1]

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Cyclic ketals are important intermediates in the chemistry of polyhydroxy compounds, notably carbohydrates, and their formation and stability are of considerable theoretical and practical interest. Acetonation of pyridoxol can conceivably

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[1] Pyridoxine Chemistry III; for preceding papers in this series, see ref. 3 and W. Korytnyk and E. J. Kris, *Chem. Ind.* (London), 1834 (1961).

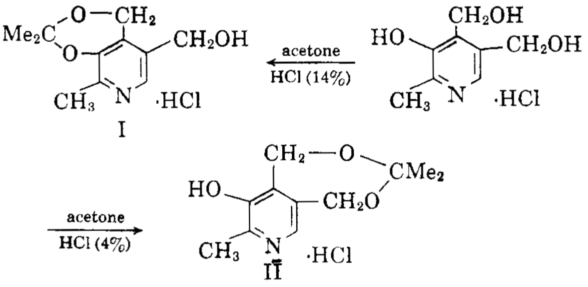
TABLE I

ULTRAVIOLET ABSORPTION SPECTRA OF PYRIDOXOL AND ITS ISOMERIC ACETONIDES

	0.1 *N* HCl		pH 6.8		0.1 *N* NaOH	
	λ_{max}	ϵ_{max}	λ_{max}	ϵ_{max}	λ_{max}	ϵ_{max}
Pyridoxol[a]	291	8.6×10^3	252	3.9×10^3	245	6.3×10^3
	232 (s)	2.1×10^3	324	7.2×10^3	310	6.8×10^3
α^4,α^5-*O*-Isopropylidenepyridoxol	288	8.6×10^{3b}	254	4.8×10^3	245	7.1×10^3
	232 (s)	2.4×10^3	318	9.4×10^3	303	7.7×10^3
α^4-3-*O*-Isopropylidenepyridoxol	290	9.0×10^3	281	5.4×10^3	281	5.45×10^3

[a] These data were taken from D. E. Metzler and E. E. Snell, *J. Am. Chem. Soc.*, **77**, 2431 (1955). [b] Heating the solution at 85° for 30-min. shifts the peak to 291 mμ (ε 9.2×10^3); at room temperature hydrolysis of isopropylidene group is very slow.

give rise to two ketals, I and II. The six-membered cyclic ketal I, usually referred to as "isopropylidenepyridoxine," is well known.[2] It has recently been obtained in quantitative yield by saturating with hydrogen chloride an acetone suspension of pyridoxol hydrochloride.[3] Using similar reaction conditions but a substantially reduced concentration of hydrogen chloride (4%), a new derivative of pyridoxol is formed, which can be readily isolated as the free base (m.p. 184–185°) in 44% yield. An increased yield (74%) was obtained when the reaction conditions were slightly modified. The new derivative has a free phenolic group (positive Gibbs' test) and a broad band at 2475 cm.$^{-1}$ (4.04 μ) in the infrared spectrum (Nujol mull), which has been assigned[4] to the $N^+—H\cdots O^-$ type of intermolecular hydrogen bonding characteristic of a number of 3-pyridols, but lacks the strong and sharp peak at 3125 cm.$^{-1}$ (3.20 μ) which is evident in I and other pyridoxine derivatives with an unsubstituted hydroxymethyl group.



The new ketal is hydrolyzed to pyridoxol hydrochloride by dilute hydrochloric acid, but is stable to alkali, a property which is quite general with cyclic ketals, including isopropylidenepyridoxine. It forms a monobenzoate (m.p. 107–109°) which is isomeric with the benzoate obtained from isopropylidenepyridoxine (m.p. 85–87°).[3] In contrast to isopropylidenepyridoxine, which did not yield a tosylate or mesylate, the new ketal could readily be monotosylated and monomesylated. Acid hydrolysis of the monotosylation product gave the *p*-toluenesulfonate of pyridoxol, in which the phenolic group is substituted.

The properties of the new acetonide are thus consistent with structure II. Following previous practice in naming these compounds, II would be O^4,O^5-isopropylidenepyridoxol, but this numbering is not completely unambiguous. Dr. Leonard T. Capell has suggested that the carbon of the methanol group be designated "α" with a superscript number for the point of attachment to the pyridine ring. Accordingly, II should be named α^4,α^5-*O*-isopropylidenepyridoxol hydrochloride, and I, α^4,3-*O*-isopropylidenepyridoxol hydrochloride.

The structure of II has been confirmed by comparison of its ultraviolet spectra with those of pyridoxol and α^4,3-*O*-isopropylidenepyridoxol (Table I). The spectrum of II at pH 6.8 and in 0.1 *N* sodium hydroxide resembles that of pyridoxol by virtue of the presence of a dissociable phenolic group giving rise to a zwitterion and an anion, respectively. On the other hand, the spectra of 3-*O*-α^4-isopropylidene pyridoxol, in which this group is substituted, are quite different. Furthermore, no shift in the ultraviolet spectrum of I or II could be observed when the buffer was saturated with boric acid at pH 6.8. This indicates[3] that either the phenolic or the α^4-hydroxy group is substituted in both compounds.

Formation of a seven-membered cyclic ketal is unusual. In the carbohydrate series, there is a pronounced tendency for the formation of five-membered cyclic ketals in preference to larger rings, and seven-membered ketals are not known.[5] Examination of atomic models of I and II indicates that both ketals are free of steric strain. However, treatment of the seven-membered ketal with hydrogen chloride under conditions suitable for the preparation of the six-membered isomer[3] gave the latter in quantitative yield. This can be taken as an indication of the greater thermodynamic stability of the six-membered ketal relative to its isomer.

The new cyclic ketal of pyridoxol should be useful as an intermediate in the modification of the 3-position of the pyridoxol molecule, and some of the possibilities are being explored in connection with

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[2] J. Baddiley and A. P. Mathias, *J. Chem. Soc.*, 2583 (1952); A. Cohen and E. G. Hughes, *ibid.*, 4384 (1952).

[3] W. Korytnyk and W. Wiedeman, *ibid.*, 2531 (1962).

[4] D. Heinert and A. E. Martell, *J. Am. Chem. Soc.*, **81**, 3934 (1959).

[5] J. A. Mills in "Advances in Carbohydrate Chemistry," Vol. X, Academic Press, Inc., New York, N. Y., 1955, p. 1.

our interest in potential antimetabolites of pyridoxine. 3-*O*-*p*-Toluenesulfonylpyridoxol was found by Dr. Charles A. Nichol to be devoid of any vitamin or antivitamin activity in *Saccharomyces carlsbergensis*.

Experimental

α^4,α^5-*O*-Isopropylidenepyridoxol.—(a). Pyridoxol hydrochloride (12.0 g., dried) was suspended in acetone (300 ml., freshly distilled). A fine stream of dry hydrogen chloride gas was passed into the suspension, the reaction mixture being kept in an ice bath. After 25 min., 13.0 g. of hydrogen chloride was taken up. The reaction mixture was shaken on a wrist action shaker for 1 hr. and was kept at −10 to −20° overnight. Filtration and washing with dry ether yielded 10.0 g. of crystalline material, which was shown by thin-layer chromatography on silica gel "G" (chloroform–methanol, 1:1) to consist of starting material and α^4,α^5-*O*-isopropylidenepyridoxol hydrochloride in about equal proportions. The mixture of the hydrochlorides was suspended in potassium carbonate solution (100 ml.), and was kept at 5° for several hours. The crude isopropylidenepyridoxol (5.4 g., 44%) had a m.p. of 165–170°, which was raised to 184–185° after crystallization from aqueous methanol.

Anal. Calcd. for $C_{11}H_{15}NO_3$: C, 63.14; H, 7.23; N, 6.69. Found: C, 63.05, H, 7.36; N, 6.60.

(b). Pyridoxol hydrochloride (12.0 g.) was suspended in acetone (250 ml.) and cooled in ice. Hydrogen chloride gas (11.0 g.) was passed into the suspension in the course of 5 min. Further processing was carried out as described in (a). The yield was 9.1 g. (74%) of crude material of m.p. 170–175; the infrared spectrum of which was essentially the same as that of authentic α^4-α^5-*O*-isopropylidenepyridoxol.

Hydrolysis of α^4,α^5-*O*-isopropylidenepyridoxol.—The ketal (0.245 g.) was dissolved in 1 *N* hydrochloric acid and was heated at 85–90° for 40 min. Water was removed on a flash evaporator, and the residue was dried. The material (0.225 g.) had a m.p. of 210–212° dec., and its infrared spectrum was indistinguishable from that of authentic pyridoxol hydrochloride.

3-*O*-Benzoyl-α^4,α^5-*O*-isopropylidenepyridoxol.—The ketal (2.415 g.) was dissolved in dry pyridine (50 ml.), cooled to 0°; and treated with benzoyl chloride (2.5 ml.). After standing for 2 hr., water (50 ml.) was added. The benzoate (3.23 g.) crystallized on standing in a refrigerator, and had a m.p. of 104–106°. Crystallization from aqueous ethanol raised the m.p. to 107–109°.

Anal. Calcd. for $C_{18}H_{19}NO_4$: C, 69.00; H, 6.10; N, 4.47. Found: C, 68.86; H, 6.43; N, 4.34.

3-*O*-*p*-Toluenesulfonyl-α^4-α^5-*O*-isopropylidenepyridoxol.—The ketal (1.05 g.) was dissolved in pyridine (50 ml.) and treated with *p*-toluenesulfonyl chloride (2.23 g.) at room temperature for 16 hr. Addition of water gave an oily product which crystallized on prolonged standing. Crystallization from ethanol yielded the pure tosylate (1.45 g.), m.p. 145–146°.

Anal. Calcd. for $C_{18}H_{21}NO_5S$: C, 59.49; H, 5.83; S, 8.80. Found: C, 59.76; H, 6.00; S, 8.96.

3-*O*-Methanesulfonyl-α^4,α^5-*O*-isopropylidenepyridoxol was similarly obtained. The mesylate had a m.p. of 72–73° after crystallization from ether–petroleum ether.

Anal. Calcd. for $C_{12}H_{17}NO_5S$: C, 50.17; H, 5.97; S, 11.17. Found: C, 49.97; H, 6.05; S, 11.29.

3-*O*-*p*-Toluenesulfonylpyridoxol was obtained by hydrolysis of *p*-toluenesulfonyl-α^4,α^5-*O*-isopropylidenepyridoxol (0.90 g.) with 10% formic acid (100 ml.) containing 20 ml. of ethanol. After heating for 30 min. on a steam bath, the solvents were removed on a flash evaporator, and the oil was crystallized from ethanol. The monotosylate (0.63 g.) had a m.p. of 184–186°, which was raised to 186–187 by two crystallizations from a mixture of chloroform and methanol.

Anal. Calcd. for $C_{15}H_{17}NO_5S$: C, 55.72; H, 5.30; S, 9.90. Found: C, 55.87; H, 5.56; S, 10.22.

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The Ultraviolet Light-Catalyzed Decomposition of N-Chlorodi-*n*-butylamine

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The effect of ultraviolet light on N-chlorodi-*n*-butylamine in carbon tetrachloride and benzene was studied in order to secure more information on the function of the sulfuric acid in the Hofmann–Löffler reaction.[1,2] The irradiation caused the precipitation of di-*n*-butylamine hydrochloride in amounts which varied with the temperature and time used. The results obtained are given in Table I.

TABLE I

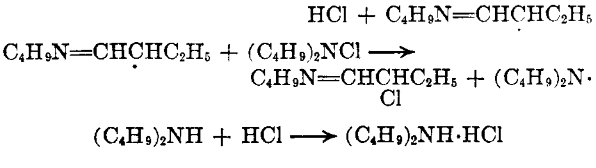
YIELDS OF DI-*n*-BUTYLAMINE HYDROCHLORIDE FORMED IN THE IRRADIATION OF N-CHLORODI-*n*-BUTYLAMINE

Temp. °C.	Time, hr.	Per cent yield[b]
25	24[a]	1.3
25	24	12.4
25	1140	47.3
6	24	11.7
77	96	55.7
25[c]	24	14.0

[a] Absence of light. [b] Basis of N-chloroamine present. [c] In benzene, the remaining runs were in carbon tetrachloride.

The carbon tetrachloride filtrate from the 1140-hour run gave after treatment with alkali only one identifiable product, *n*-butylamine, which was isolated and identified as *n*-butylbisbenzenesulfonimide.

The products obtained parallel those obtained by Wright[3] in the thermal decomposition of N-chlorodi-*n*-butylamine and are formed by the following free radical mechanism



$$(C_4H_9)_2NCl \xrightarrow{h\nu} (C_4H_9)_2N\cdot + Cl\cdot$$

$$2(C_4H_9)_2N\cdot \longrightarrow (C_4H_9)_2NH + C_4H_9N{=}CHCH_2C_2H_5$$

$$Cl\cdot + C_4H_9N{=}CHCH_2C_2H_5 \longrightarrow HCl + C_4H_9N{=}CH\underset{\cdot}{C}HC_2H_5$$

$$C_4H_9N{=}CH\underset{\cdot}{C}HC_2H_5 + (C_4H_9)_2NCl \longrightarrow C_4H_9N{=}CH\underset{Cl}{C}HC_2H_5 + (C_4H_9)_2N\cdot$$

$$(C_4H_9)_2NH + HCl \longrightarrow (C_4H_9)_2NH\cdot HCl$$