with chloroform, melted at 174–175° (a later trial gave material of m.p. 178–179°) and had a neutral equivalent of 63 (calcd. for succinic acid, 59). A mixed m.p. with pure succinic acid, m.p. 188°, was 184–188°. Concentration of the yellow chloroform washings yielded a small amount of white solid, m.p. 148–152°; neutral equivalent 74 (calcd. for adipic acid, 73). A mixed m.p. with adipic acid, m.p. 152°, was 148–152°. Further evaporation gave a yellow solid slightly soluble in cold benzene, ether and chloroform, but readily soluble in water and hot organic solvents. Four crystallizations of this material from benzene and chloroform gave a small quantity of γ-ketoazelaic acid, m.p. 110–111° (lit.,[38] 108–109°); neutral equivalent 100 (calcd. for γ-ketoazelaic acid, 101). Its semicarbazone, microcrystals from water, melted at 197–198° (dec.) (lit.,[38] 197°). Mixed m.p.'s of the ketoazelaic acid and the semicarbazone with available authentic samples were 109.5–111° and 196.5–198°, respectively.

Ultraviolet Absorption Spectra of Indans.—Table I summarizes the ultraviolet data on the indans prepared in this work. The spectra vary sufficiently to make possible the differentiation of indans unsubstituted in the aromatic nucleus, 4-alkyl derivatives and 5-alkyl derivatives. Of interest is the comparison of these data with those of the corresponding methylbenzenes. The spectra are parallel, with the indans absorbing at wave lengths 2–5 mμ higher than the alkyl benzenes, as indicated by the last column of Table I taken from the work of Conrad-Billroth.[39]

(38) Brown and Farmer, *Biochem. J.*, **29**, 631 (1935).

Summary

Two synthetic routes to the substituted octahydrocoumarins have been investigated, one using the Mannich bases of cyclohexanones and the other involving the cyanoethylation of cyclohexanones. Octahydrocoumarin and the 6-, 8- and 10-methyloctahydrocoumarins have been prepared by these methods.

These four octahydrocoumarins have been treated with phosphorus pentoxide, the products characterized and the reactions discussed. Octahydrocoumarin is converted to 4,5,6,7-tetrahydroindanone and indan, 8-methyloctahydrocoumarin to 7-methyl-4,5,6,7-tetrahydroindanone and 4-methylindan, 6-methyloctahydrocoumarin to 5-methyl-4,5,6,7-tetrahydroindanone and 5-methylindan and 10-methyloctahydrocoumarin to 4-methylindan.

(39) Conrad-Billroth, *Z. physik. Chem.*, **B29**, 170 (1935).

URBANA, ILLINOIS RECEIVED AUGUST 8, 1950

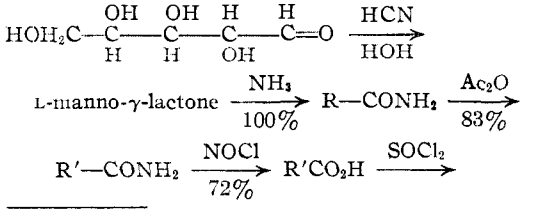
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE OHIO STATE UNIVERSITY]

L-Mannoheptulose (L-Manno-L-*tagato*-heptose)[1]

BY M. L. WOLFROM AND HARRY B. WOOD

In extension of our previous work on ketose synthesis, we herein describe the synthesis of a new ketoheptose, L-mannoheptulose (L-manno-L-*tagato*-heptose). This is the enantiomorph of D-mannoheptulose, the naturally occurring ketoheptose isolated by LaForge[2] from the fruit of the avocado tree (*Persea gratissima* Gaert.). D-Mannoheptulose ("mannoketoheptose") has been synthesized: by Montgomery and Hudson[3] from D-manno-D-*gala*-heptose through alkaline rearrangement; by Sowden[4] from D-arabinose through condensation with the sodium salt of 2-nitroethanol and subsequent hydrolysis; and by Ettel and Liebster[5] from natural volemitol (D-manno-D-*talo*-hepitol) by oxidation with *Acetobacter suboxydans* (though not with *Acetobacter xylinum*[6]).

In this work, L-mannoheptulose has been synthesized from L-arabinose through the reactions



(1) Paper No. 13 in the series entitled "The Action of Diazomethane upon Acyclic Sugar Derivatives"; previous communication, M. L. Wolfrom and P. W. Cooper, THIS JOURNAL, **72**, 1345 (1950).

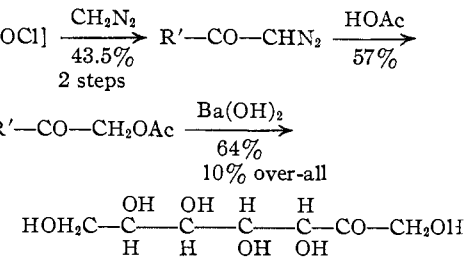
(2) F. B. LaForge, *J. Biol. Chem.*, **28**, 511 (1917).

(3) Edna M. Montgomery and C. S. Hudson, THIS JOURNAL, **61**, 1654 (1939).

(4) J. C. Sowden, *ibid.*, **73**, 3325 (1950).

(5) V. Ettel and J. Liebster, *Collection Czechoslov. Chem. Communs.*, **14**, 80 (1949).

(6) Laura C. Stewart, N. K. Richtmyer and C. S. Hudson, THIS JOURNAL, **71**, 3532 (1949).



The procedure of Kiliani[7] was employed in converting natural L-arabinose to L-mannono-γ-lactone. In crystallizing this lactone from ethanol, a considerable quantity of ethyl L-mannonate was obtained in crystalline condition. It would thus appear that mannonic acid has some stability in its acyclic form, albeit the ester may be easily converted[8] to the lactone. The enantiomorph of this ester has been reported by Nef and Hedenburg[8] who encountered it in their classical studies on the γ and δ forms of D-mannonolactone.

L-Mannonamide was found by us to be surprisingly hydrolytically unstable (see Fig. 1). To our knowledge, this behavior has not been reported previously. The polarimetric data of Fig. 1 would indicate that the final product in solution is mainly the ammonium salt. Recently, Hockett and co-workers[9] recommended that aldonamides be recrystallized from methyl cellosolve (ethylene glycol monomethyl ether) to avoid hydrolysis.

(7) (a) H. Kiliani, *Ber.*, **19**, 3033 (1886); (b) **55**, 100 (1922).

(8) J. U. Nef (and O. Hedenburg), *Ann.*, **403**, 316 (1914); O. F. Hedenburg (and J. U. Nef), THIS JOURNAL, **37**, 345 (1915).

(9) R. C. Hockett, J. B. Ames, H. A. Hill and A. Scattergood, *Abstracts Papers Am. Chem. Soc.*, **114**, 3Q (1948); R. C. Hockett, private communication.

The enantiomorph of L-mannonamide O-pentaacetate[10] and of L-mannonic acid pentaacetate monohydrate[11] had been reported previously. Pentaacetyl-L-mannonyl chloride was not crystallized. Chromatography was required to obtain the pure diazomethyl ketone but moderately pure material was satisfactory for the next step. Methyl pentaacetyl-L-mannonate is described.

keto-L-Mannoheptulose hexaacetate was not enantiomorphous with the D-mannoheptulose hexaacetate reported by Montgomery and Hudson[8]; the latter is therefore a ring structure. This conclusion had also been reached by Montgomery and Hudson on comparison of optical rotatory data for D-mannoheptulose and derivatives with those of corresponding members of the D-mannose series and on this basis an α-D-pyranose assignment was made to this hexaacetate. The fact that the α-D-hexaacetate underwent normal acetohalogen formation also augurs for such a structure.

L-Mannoheptulose crystallized in beautiful prisms that were enantiomorphous with D-mannoheptulose. Its phenylosazone and racemate were prepared.[12] The fact that the X-ray powder diffraction diagram of the racemate was identical with that of L-mannoheptulose (Table I) demonstrates that this racemate is a mechanical mixture of enantiomorphs and not a true racemic compound. On the other hand, the X-ray diffraction pattern of D,L-mannonamide is different from that of its components (Table I) and it is therefore a racemic compound. The enhanced melting point (140–141°) exhibited by D,L-mannonamide O-pentaacetate over that of its components (m. p. 108–110°) makes it probable that this substance is likewise a true racemic compound.

TABLE I

X-RAY POWDER DIFFRACTION PATTERNS[a] OF MANNOHEPTULOSE, ITS TWO HEXAACETATES, MANNONAMIDE AND D,L-MANNONAMIDE[b]

D-, L- or D,L-Mannoheptulose		*keto*-L-Mannoheptulose hexaacetate		α-D-Mannoheptulopyranose hexaacetate[d]		L-Mannonamide		D,L-Mannonamide	
I-P-S,[c] Å.	*I*[e]	I-P-S, Å.	*I*	I-P-S, Å.	*I*	I-P-S, Å.	*I*	I-P-S, Å.	*I*
5.57	8	7.18	9	7.43	8	4.82	10	4.86	8
4.72	9	6.22	6	5.66	10	4.37	9	4.33	10
3.91	10	4.49	10	4.60	6	3.80	4	3.61	3
3.52	1	4.04	7	4.14	9	3.37	8	3.42	4
3.07	6	3.48	8	3.78	7	3.06	3	3.27	2
2.95	1	3.23	3	3.46	5	2.87	5	3.13	1
2.83	3	3.05	4	3.19	3	2.61	1	2.97	6
2.69	7	2.86	5	2.98	1	2.35	7	2.68	5
2.39	4	2.66	1	2.74	4	2.14	6	2.52	1
2.27	5	2.42	2	2.45	1	1.93	1	2.37	9
2.20	1	2.08	1	2.29	2	1.71	2	2.26	1
2.04	2	1.96	1	2.17	1	1.57	1	2.18	1
1.83	1			1.93	1			2.08	7
1.75	1			1.74	1			1.97	1
1.71	1							1.81	1
1.57	1								
1.53	1								
1.44	1								
1.40	1								

[a] Filtered CuKα radiation, effectively 1.5418 Å.; film exposure two hours; no back reflections observed. [b] Acknowledgment is made to Professor P. M. Harris and to Gwendolyn B. Wood for assistance in obtaining these data. [c] Interplanar spacings. [d] See ref. 12. [e] Relative intensity, estimated visually: 10, strongest band; 1, weakest band.

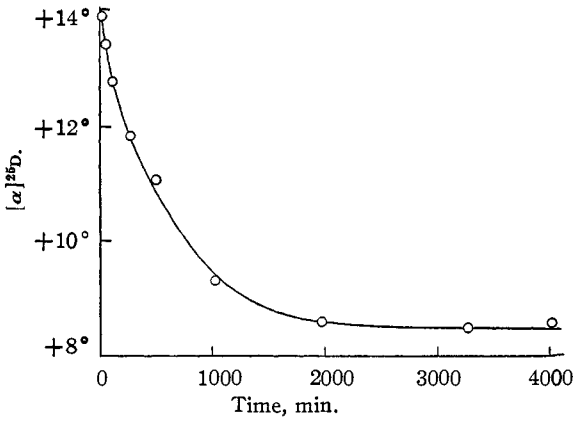


Fig. 1.—Mutarotation of L-mannonamide in water (*c*, 1.6) at 25°, *p*H change: 8.4 → 8.9 (1 min.) → 8.0 (final); *p*H change at 60°: 8.4 → 8.5 (2 min.) → 5.2 (final). Since P. A. Levene and G. M. Meyer, *J. Biol. Chem.*, **26**, 335 (1916), cite $[\alpha]^{20}D$ −8.8° (*c*, 9.5, water) for sodium D-mannonate, the final rotation is therefore that of the anion.

Experimental

Ethyl L-Mannonate.—L-Arabinose (192 g.) was treated with hydrocyanic acid according to the procedure of Kiliani.[7] After hydrolysis with barium hydroxide, the cations were removed with an exchange resin (Amberlite IR-100-H[12a]) and the effluent was concentrated under reduced pressure to a thick sirup from which water was removed by azeotroping with ethanol. The sirup was dissolved in hot ethanol (200 ml.) and L-mannono-γ-lactone crystallized on seeding; yield 56.2 g. (50.8 g., m.p. 148–150°, $[\alpha]^{26}D$ −50° (*c*, 3, water, initial); 5.4 g., m.p. 148°, $[\alpha]^{26}D$ −48° (*c*, 3, water, initial), obtained on concentration to *ca.* 125 ml. Concentrating a second time to *ca.* 75 ml. gave a crop of essentially pure ethyl L-mannonate; yield 18.1 g. (6.4%, basis L-arabinose), m.p. 157–160°, $[\alpha]^{22}D$ −1° (*c*, 2, water, initial). For the enantiomorph, Nef[8] reports m.p. 164°, $[\alpha]^{20}D$ 0° (water).

Anal. Calcd. for $C_8H_{16}O_7$: C, 42.75; H, 7.19. Found: C, 42.57; H, 7.06.

L-Mannonamide.—This was prepared in nearly quantitative yield from L-mannono-γ-lactone and liquid ammonia according to the procedure of Glattfeld and Macmillan.[13] The crystalline product was dried over phosphorus pentoxide at room temperature and under reduced pressure; m.p. 170–171° (dec.), $[\alpha]^{25}D$ +14° (*c*, 1.6, water, initial extrapolated value), in reasonable agreement with the values (m.p. 176–177°, $[\alpha]^{20}D$ −13° in water) cited by Glattfeld and Macmillan[13] for the enantiomorph. Kiliani[7a] and Weerman[14] had previously reported this enantiomorph in impure form. Figure 1 demonstrates the hydrolytic instability of this compound; its X-ray powder diffraction lines are recorded in Table I.

Anal. Calcd. for $C_6H_{13}O_6N$: C, 36.95; H, 6.71; N, 7.18. Found: C, 36.94; H, 6.94; N, 7.28.

D,L-Mannonamide.—An amount of 1.0000 g. of each of the enantiomorphs was dissolved in liquid ammonia. The

(10) G. B. Robbins and F. W. Upson, THIS JOURNAL, **60**, 1788 (1938).

(11) M. L. Wolfrom, M. Konigsberg and D. I. Weisblat, *ibid.*, **61**, 576 (1939).

(12) We are indebted to C. S. Hudson, U. S. Public Health Service, Bethesda, Maryland, for a sample of natural D-mannoheptulose.

(12a) Resinous Products & Chemical Co., Philadelphia, Pennsylvania.

(13) J. W. E. Glattfeld and D. Macmillan, THIS JOURNAL, **56**, 2481 (1934).

(14) R. A. Weerman, *Rec. trav. chim.*, **37**, 33 (1918).

crystalline solid obtained on solvent evaporation was dried at 25° over phosphorus pentoxide and under reduced pressure; m.p. 155–156° (dec.). The X-ray powder diffraction lines (Table I) for this substance are different from those of its components and it is thus a racemic compound.

Anal. Calcd. for $C_6H_{13}O_6N$: C, 36.95; H, 6.71; N, 7.18. Found: C, 36.68; H, 6.40; N, 7.27.

L-Mannonamide O-Pentaacetate.—L-Mannonamide (10 g.) was acetylated with acetic anhydride and zinc chloride according to the procedure of Robbins and Upson[10] for the enantiomorph and the product was crystallized from ethylene glycol butyl ethyl ether; yield 17.4 g. (83%), m.p. 108°. Pure material was obtained on recrystallization from the same solvent; m.p. 110–110.5°, $[\alpha]^{23}D$ −38.3° (*c*, 3.5, chloroform[15]). For the enantiomorph, Robbins and Upson[10] cite m.p. 110°, $[\alpha]^{25}D$ +38.7° (*c*, 1.8, chloroform).

Anal. Calcd. for $C_{16}H_{23}O_{11}N$: C, 47.41; H, 5.71; N, 3.45. Found: C, 47.48; H, 5.42; N, 3.41.

D,L-Mannonamide O-Pentaacetate.—This substance was prepared by crystallization of equal amounts (0.200 g.) of the enantiomorphs from ethylene glycol butyl ethyl ether (4 ml.); m.p. 140–141°, $[\alpha]^{24}D$ 0° (chloroform).

L-Mannonic Acid O-Pentaacetate Monohydrate.—L-Mannonamide O-pentaacetate (10 g.) was deaminated with nitrosyl chloride as described[11] for the enantiomorph and the product was crystallized in the same manner; yield 7.5 (72%), m.p. 68–70°. Pure material resulted on recrystallization from ethanol–water; m.p. 70–70.5°, $[\alpha]^{24}D$ −23° (*c*, 1.6, chloroform). Reported[11] constants for the enantiomorph are m.p. 68–70°, $[\alpha]^{21}D$ +23° (*c*, 1.6, U. S. P. chloroform). All attempts to secure this acid in the crystalline anhydrous form failed.

Anal. Calcd. for $C_{16}H_{22}O_{12}\cdot H_2O$: C, 45.30; H, 5.71; H_2O, 4.23. Found: C, 45.28; H, 5.58; H_2O,[16] 4.03.

Methyl Pentaacetyl-L-mannonate.—To a 2% solution of diazomethane in ether (15 ml.) was added L-mannonic acid pentaacetate monohydrate (1.2 g.) and the solution was kept overnight at ice-box temperature. The diazomethane was removed by repeated ether addition and distillation. Crystallization was effected by the addition of petroleum ether; yield 1.1 g., m.p. 77–79°. Pure material was obtained on recrystallization from methanol–ether–petroleum ether; m.p. 79–80°, $[\alpha]^{27}D$ −19° (*c*, 3.3, chloroform).

Anal. Calcd. for $C_{17}H_{24}O_{12}$: C, 48.57; H, 5.76. Found: C, 48.60; H, 5.73.

1-Diazo-1-desoxy-*keto*-L-mannoheptulose Pentaacetate.—L-Mannonic acid pentaacetate monohydrate (9 g.) was dehydrated by azeotroping repeatedly with benzene. The resulting clear sirup was dissolved in 50 ml. of anhydrous benzene and 12 ml. of thionyl chloride (purified by the method of Cottle[17]) was added. This solution was maintained at reflux temperature until only a faint positive test for hydrochloric acid was noted using ammonia solution at the top of the reflux condenser. The thionyl chloride was removed by solvent concentration under reduced pressure followed by repeated additions of benzene and subsequent removal in the same manner. The resultant sirup was dissolved in 50 ml. of anhydrous ether, cooled to 10° and slowly added to a solution of 2.2 g. (2.5 moles per mole of acid) of diazomethane gas dissolved in 200 ml. of anhydrous ether, whereupon a vigorous evolution of gas ensued. The reaction mixture was allowed to stand overnight at 0°, some separated polymethylenes were removed by filtration and the filtrate was reduced to one-third volume by distillation. The solution was treated with charcoal and beautiful elongated prisms separated on solvent concentration; yield 4 g. (43.5%), m.p. 73–75°. Repeated recrystallizations from ethanol–water or warm ether did not yield pure material.

Two grams of the above product was dissolved in 20 ml. of benzene and chromatographed on a 230 × 35 mm. (diam.)[18] column of Magnesol[19]–Celite[20] (5:1 by wt.) by development with 750 ml. of benzene–ethanol (100:1 by vol.). An alkaline permanganate streak[21] showed a large zone near the bottom of the extruded column and a faint one near the top. The sectioned bottom zone was extracted with acetone and the sirup obtained on solvent removal was recrystallized from warm ether. The needle-like crystalline mass possessed a slight yellow tinge; yield 1.2 g., m.p. 75–76°, $[\alpha]^{26}D$ −12° (*c*, 4, chloroform).

Anal. Calcd. for $C_{17}H_{22}O_{11}N_2$: C, 47.44; H, 5.15; N, 6.50. Found: C, 47.30; H, 5.02; N, 6.30.

***keto*-L-Mannoheptulose Hexaacetate.**—A solution of 1-diazo-1-desoxy-*keto*-L-mannoheptulose pentaacetate (5.1 g.) in 75 ml. of glacial acetic acid,[22] to which had been added 0.01 g. of cupric acetate, was heated to 80–90° where the solution changed color from green to yellow and a vigorous evolution of nitrogen occurred. The reaction mixture was brought to reflux and maintained there for 5 minutes. The cooled solution was then poured into 200 ml. of ice and water, extracted with chloroform (decolorizing charcoal) and dried over anhydrous sodium sulfate. The residue obtained on solvent removal under reduced pressure was crystallized as fine needles from warm ether (10 ml.); yield 3.1 g. (57%); m.p. 93–94°.

The filtrate was concentrated under reduced pressure to a sirup which was dissolved in 5 ml. of benzene and chromatographed on a 230 × 35 mm. (diam.) column[18] of Magnesol[19]–Celite[20] (5:1 by wt.) by development with 600 ml. of benzene–ethanol (100:1 by vol.). The principal zone near the bottom was detected by the alkaline permanganate streak[21] and on elution with acetone gave crystalline material; yield 0.47 g., m.p. 94–95°.

Recrystallization from warm ether or ethanol–water gave pure material; m.p. 97–98°, $[\alpha]^{23}D$ −3.6° (*c*, 2, chloroform). The acetate was readily soluble in chloroform, moderately so in ether and was insoluble in petroleum ether or water. It reduced warm Benedict solution and exhibited an absorption band with a maximum at 2870 Å.; log $\epsilon_{max.}$[23] 1.77 (0.0173 *M* in chloroform, 1-cm. cell, Beckman quartz spectrophotometer, model DU). The X-ray powder diffraction data for this substance are recorded in Table I and are therein compared with those for the isomeric D-mannoheptulose hexaacetate (m.p. 110°, $[\alpha]^{20}D$ +39° in chloroform) described by Montgomery and Hudson.[3]

Anal. Calcd. for $C_{19}H_{26}O_{13}$: C, 49.35; H, 5.63. Found: C, 49.32; H, 5.44.

L-Mannoheptulose (L-Manno-L-*tagato*-heptose).—*keto*-L-Mannoheptulose hexaacetate (6 g.) was deacetylated as described previously for *keto*-D-psicose pentaacetate.[24] Ion exchange resins Amberlite[12] IR-100-H and IR-4-B were employed. The sirup obtained on water removal was crystallized from 20 ml. of absolute ethanol; yield 1.5 g., m.p. 150–151°, $[\alpha]^{21}D$ −29° (*c*, 2.7, water, no mutarotation). Accepted constants[2,3] for the enantiomorph are m.p. 152°, $[\alpha]^{20}D$ +29° (*c*, 2, water). This ketose formed beautiful, large prismatic crystals whose X-ray powder diffraction lines are recorded in Table I. It possessed a sweet taste and reduced Benedict solution.

Anal. Calcd. for $C_7H_{14}O_7$: C, 40.00; H, 6.70. Found: C, 40.00; H, 6.58.

The mother liquors from the L-mannoheptulose crystallization were subjected to phenylosazone formation; yield 0.4 g. (≈ 0.25 g. of mannoheptulose or a total ketose yield of 1.75 g., 64%). Recrystallization from ethanol–water yielded L-*manno*-heptose phenylosazone; m.p. 197°. This osazone has been prepared from L-manno-L-*gala*-heptose by Smith,[25] who records a melting point of *ca.* 203° (dec.).

Anal. Calcd. for $C_{19}H_{24}O_5N_4$: C, 58.73; H, 6.23; N, 14.43. Found: C, 58.76; H, 5.92; N, 14.28.

D,L-Mannoheptulose.—This compound was obtained by recrystallizing a mixture of equal amounts (0.1000 g.) of the enantiomorphs[12] from 95% ethanol; m.p. 135–136°; $[\alpha]^{26}D$ 0° (*c*, 2, water). This product showed the same X-ray

(15) All chloroform used in polarizations contained *ca.* 0.5% ethanol.

(16) Loss in weight on heating at 110° under reduced pressure over phosphorus pentoxide.

(17) D. L. Cottle, THIS JOURNAL, **68**, 1380 (1946).

(18) Adsorbent dimensions.

(19) Westvaco Chlorine Products Co., South Charleston, West Virginia.

(20) No. 535, Johns-Manville Co., New York, N. Y.

(21) W. H. McNeely, W. W. Binkley and M. L. Wolfrom, THIS JOURNAL, **67**, 527 (1945).

(22) Purified by refluxing over potassium permanganate, distilling and drying with Drierite (calcium sulfate as soluble anhydrite).

(23) $\epsilon_{max.} = E_{max.} \times$ mol. wt./$C \times D$; C = g./l., D = cell thickness in cm.

(24) M. L. Wolfrom, A. Thompson and E. F. Evans, THIS JOURNAL, **67**, 1793 (1945).

(25) W. S. Smith, *Ann.*, **272**, 182 (1893).

powder diffraction pattern as that for either the D- or L-mannoheptulose alone (Table I), thereby proving it to be a racemic mixture rather than a true racemic compound.

Summary

1. The synthesis of L-mannoheptulose from L-arabinose is described.

2. D,L-Mannoheptulose is prepared and demonstrated to be a racemic mixture.

3. Mannonamide is hydrolytically unstable in aqueous solution.

4. The following substances are also described in crystalline condition: ethyl L-mannonate; L-mannonamide (in pure form); D,L-mannonamide (shown to be a racemic compound); the O-pentaacetates of the L and D,L (shown to be a racemic compound) forms of mannonamide, of L-mannonic acid monohydrate and of methyl L-mannonate; 1-diazo-1-desoxy-*keto*-L-mannoheptulose pentaacetate; and *keto*-L-mannoheptulose hexaacetate.

COLUMBUS, OHIO RECEIVED AUGUST 22, 1950

[CONTRIBUTION FROM THE DIVISION OF AGRICULTURAL BIOCHEMISTRY, UNIVERSITY OF MINNESOTA]

The Preparation of a Reversible Oxidation Product of α-Tocopherol, α-Tocopheroxide and of Related Oxides[1]

BY PAUL D. BOYER

The oxidation of α-tocopherol (I) by ferric or auric chloride or by silver nitrate has been shown to give α-tocopherylquinone (IV),[2] which has hitherto been regarded as the first oxidation product stable enough to be isolated. This paper records the isolation and tentative characterization of an intermediate, biologically active,[3] reversible oxidation product of α-tocopherol which has been designated as "α-tocopheroxide." In addition there is reported herein the preparation of oxides of β-, γ- and δ-tocopherols, oxides of *p*-xylohydroquinone and durohydroquinone monoalkyl ethers and of duroquinone dioxide.

The initial observations which indicated that a well-defined intermediate product was formed in the conversion of α-tocopherol to α-tocopherylquinone were made during a study of the oxidation of α-tocopherol in 95% ethanol by ferric chloride in the presence of 2,2′-bipyridine. Addition of L-ascorbic acid to the reaction mixture immediately after oxidation of the α-tocopherol was found to yield a product which resembled α-tocopherol and not α-tocopherylhydroquinone or α-tocopherylquinone in its properties. As measured by the color of the ferrous iron-2,2′-bipyridine complex, the initial oxidation involved the transfer of two electrons per α-tocopherol molecule. It was therefore apparent that the observations were not due to the formation of a free radical of α-tocopherol, such as recently has been demonstrated by Michaelis and Wollman.[4]

Subsequent experiments led to the isolation of α-tocopheroxide as a labile colorless oil which under mildly acid conditions was readily converted irreversibly to α-tocopherylquinone or which could be reduced by ascorbic acid or sodium hydrosulfite to α-tocopherol. That the product obtained upon reduction of α-tocopheroxide with ascorbic acid was α-tocopherol was shown by the identity of the reduction product and of authentic α-tocopherol with respect to the ultraviolet absorption spectrum, total reducing potency, rate of reaction with ferric chloride and 2,2′-bipyridine, nature of the products formed by oxidation and the formation of the 3,5-dinitrophenylurethan derivative[5] which melted at 142–144° alone or when mixed with the derivative from an authentic sample of *d,l*-α-tocopherol.

Oxidation of α-tocopherol by ferric iron is known to be slow in the absence of 2,2′-bipyridine.[6] When tocopherol was oxidized by ferric iron without 2,2′-bipyridine present the chief product obtained was α-tocopherylquinone. If excessive amounts of 2,2′-bipyridine were used, the α-tocopheroxide contained more extraneous products other than α-tocopherylquinone. The 2,2′-bipyridine modifies the reaction probably through regulation of the acidity of the medium as well as by forming a complex with ferrous iron.

Characterization of the α-tocopheroxide was of interest both because of the possible biological importance of the compound and the lack of any readily apparent structure for an intermediate between α-tocopherol and α-tocopherylquinone.

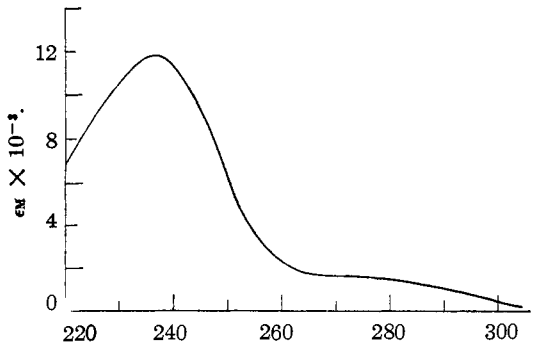


Fig. 1.—The ultraviolet absorption spectrum of α-tocopheroxide in isoöctane.

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