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A NOVEL DEGRADATION PATHWAY OF L-ASCORBIC ACID (1)

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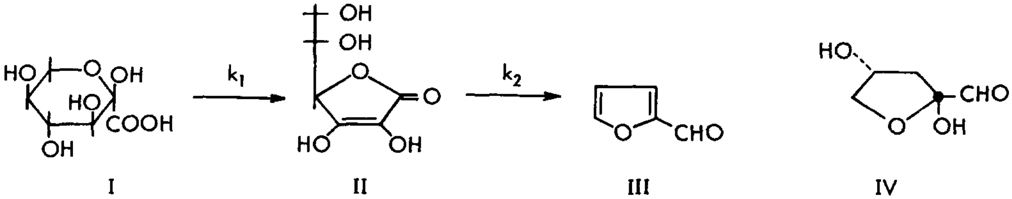
The degradation pathway of L-ascorbic acid (II) is still not so clear. Regna and Caldwell have reported that the reaction of L-xylo-2-hexulosonic acid (I) in 5M HCl can be generalized into equation of $I \xrightarrow{k_1} II \xrightarrow{k_2}$ 2-furaldehyde (III), since it is a consecutive process of the first order (2). Yamamoto and Yamamoto have obtained the same result at pH 1.7 and concluded that the anaerobic degradation of II in weakly acidic solution does not proceed via I as an intermediate (3). Recently, Kurata and Sakurai have successfully isolated 3-deoxy-L-threo-2-pentosulose (IV) in an acid-catalyzed degradation of II and presented a novel pathway of II → I → IV → III (4). However, their conclusion seems to be inconflict with the above. Our preceding paper further suggested that there could be not much possibility of existence of I as a major intermediate (5). This paper reports a novel intermediate of the degradation.



At the outset, kinetic studies on the reaction of I were carried out in wide acid concentration ranges, 0.5-10M HCl and the same conclusion with Regna and Yamamoto was obtained. Data are shown in Table I. A linear relationship exists between log k_1 and $-H_0$ and between log k_2 and log C_{HCl}. Values of w and w* (6) shown in Table II suggest an important role of water in transition states. These kinetic data strongly support the degradation pathway of I → II → III. On such a pathway, Cier and his coworkers have presented an interesting one, though it is not experimentally proved (7).

To present a reliable pathway, the degradation of II in methanol was attempted. When II in methanol

Table I. Rate Coefficients (k_1 and k_2) at 70°

	C_{HCl} [M]					
	0.5 (-0.20)[a]	1.0 (0.20)[a]	3.0 (1.05)[a]	5.0 (1.76)[a]	8.0 (3.00)[a]	10.0 (3.68)[a]
k_1	1.12×10^{-5}	2.17×10^{-5}	6.67×10^{-5}	1.50×10^{-4} (1.37×10^{-4})[b]	5.00×10^{-4}	1.07×10^{-5}
k_2	8.26×10^{-6}	1.14×10^{-5}	1.93×10^{-5}	2.31×10^{-5} (2.35×10^{-5})[b]	3.14×10^{-5}	3.62×10^{-5}

a: $-H_0$ b: data by Regna (2)

Table II. Values of w and w*

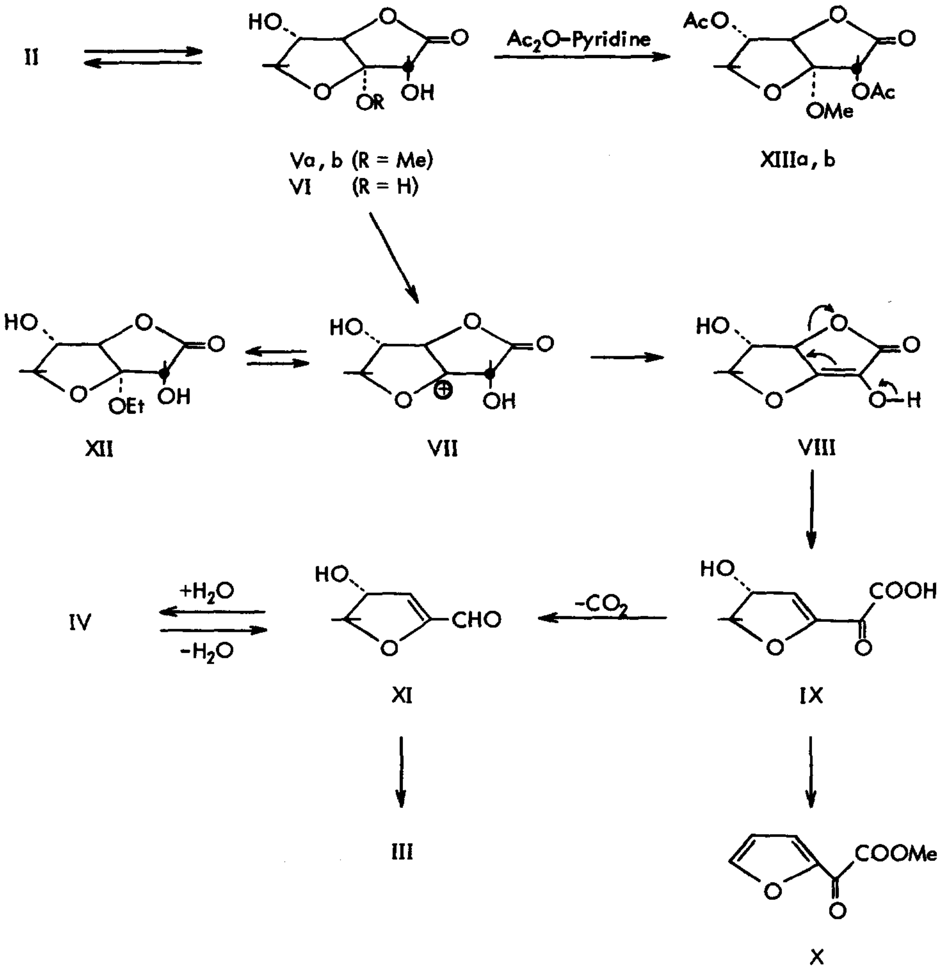
	w	w*
k_1	+3.56	-1.34
k_2	+5.96	+1.03

was refluxed in the presence of boron trifluoride-etherate for 10 hr, Va, Vb and X (5) were detected as major products. Products were isolated by preparative TLC and II was recovered to some extent.

The IR spectrum of Va, $C_7H_{10}O_6$, shows the characteristic bands due to a hydroxy group and saturated γ-lactone. The NMR spectrum of the acetate of Va (XIIIb) shows three 3-proton singlets due to one methoxy and two acetoxy groups, one 1-proton singlet due to H_2 and signals appearing as the pattern of ABXY system due to H_6, H_6', H_5 and H_4. Therefore, the structure of Va was established. As similar data were obtained about Vb, Vb was determined as the C_2-epimer of Va. Determination of the configurations of C_2-OH groups of both compounds is now in progress.

It is quite natural to consider that the configuration of methoxy group of V should be α, since a cis-form is more stable in bicyclo[3.3.0]octanes (8). The CD curve of V showing + Cotton effect also supports this idea (9). Exchange of the methoxy group at C_3 with an ethoxy group, the formation of XII, was easily achieved by the heating of Va in ethanol with boron trifluoride-etherate. The treatment of Va with potassium carbonate in methanol, followed by neutralization with Amberlite IR 120 (H^+), afforded 3-O-methyl-L-ascorbic acid (10). These results also supported the structure of V.

Further heating of V with boron trifluoride-etherate gave X (5). The corresponding C_2-epimer of V



and II were isolated as minor products, but no other components were detected. Therefore, the reaction of II in methanol is concluded to proceed via the pathway of II → V → VII → VIII → IX → X. This conclusion suggests that the acid-catalyzed degradation of II in water will proceed via the pathway of II → VI → VII → VIII → IX → XI → III and the compound IV isolated by Kurata and Sakurai (4) will be formed by the addition of water to XI.

Data of new compounds are reported below (chemical shifts and IR spectral data are expressed in τ value and wave number, respectively) (11).

Va: mp 167-169°. $[\alpha]_D^{26}$ +2.7 (c 1.031 MeOH). IR nujol 3480, 3390 (OH), 1790 (C=O).

Vb: mp 94-95°. $[\alpha]_D^{21.5}$ +73.9 (c 1.016 MeOH). IR nujol 3360, 3160 (OH), 1780 (C=O).

XIIIa: mp 105-106°. $[\alpha]_D^{21.0}$ +58.9 (c 1.025 $CHCl_3$). IR nujol 1806, 1740 (C=O). NMR ($CDCl_3$) 7.89^s, 7.77^s,(6H, OAc), 6.62^s (OMe), 6.00^q ($H_{6'}$, $J_{6,6'}$ 10.0 Hz), 5.50^q (H_6), 4.79^m (H_5, $J_{4,5}$ 0.5 Hz), 5.25^d (H_4), 4.27^s (H_2).

XIIIb: mp 98.5-100°. $[\alpha]_D^{26}$ +155.8 (c 1.053 $CHCl_3$). IR nujol 1788, 1750 (C=O). NMR ($CDCl_3$) 7.90^s, 7.84^s (6H, OAc), 6.63^s (OMe), 6.12^q ($H_{6'}$, $J_{6,6'}$ 10.0 Hz), 5.49^q (H_6), 4.97^m (H_5, $J_{4,5}$ 0.5 Hz), 5.02^d (H_4), 5.03^s (H_2).

XII (obtained from Va): mp 144-145.5°. $[\alpha]_D^{21.0}$ -2.5 (c 1.021 MeOH). IR nujol 3570, 3450 (OH), 1815 (C=O).

The acetate of XII: syrup. $[\alpha]_D^{20}$ +48.2 (c 0.901 $CHCl_3$). IR CCl_4 1815, 1715 (C=O).

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