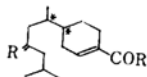


*The Structure of Todomatuic Acid. Synthesis of  
(±)-Dihydro-desoxo-todomatuic Acid*

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(Received March 6, 1961)

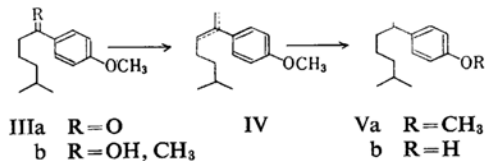
Todomatuic acid,  $C_{15}H_{24}O_3$ , monocyclic unsaturated keto-acid (m. p.  $58.5^\circ\text{C}$ , b. p.  $200\sim 215^\circ\text{C}/3\text{ mmHg}$ ,  $[\alpha]_D^{25} + 85.84^\circ$ ; semicarbazone, m. p.  $193.2\sim 193.7^\circ\text{C}$ ), was first isolated by Tuchihasi and Hanzawa<sup>1)</sup> on hydrolysis of the high boiling fraction of an oil, obtained as a by-product when *Abies sachalinensis* Mast. (to do matu) was digested with sulfite in pulp industry.



- Ia R=O R'=OH  
b R=H<sub>2</sub> R'=OH  
c R=H<sub>2</sub> R'=OCH<sub>3</sub>

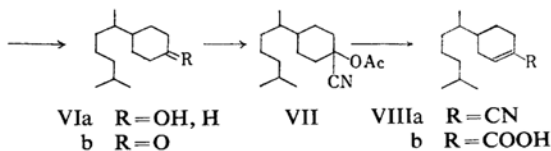
The structure Ia was advanced by Momose<sup>2)</sup>, mainly by the results of oxidative degradation of Ia with potassium permanganate which gave oxalic acid and an acyclic saturated ketodicarboxylic acid (II),  $C_{13}H_{22}O_5$  (semicarbazone, decomp. p.  $185\sim 186^\circ\text{C}$ ). Further oxidation of II with nitric acid gave isovaleric acid and  $\beta$ -( $\alpha$ -carboxyethyl)glutaric acid. Among various possible structures which satisfy the results of the degradation, Ia was favored because Ia is compatible with the isoprene rule.

In this communication, the synthesis of (±)-dihydro-desoxo-todomatuic acid (Xb) is reported.

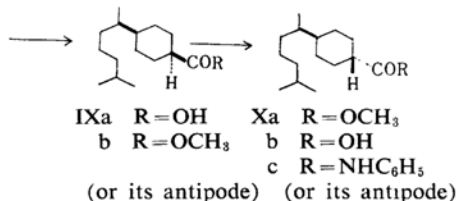


(4-Anisyl)-isohexyl ketone (IIIa) (b. p.  $131\sim 133^\circ\text{C}/1\text{ mmHg}$ ; semicarbazone, m. p.  $124\sim 125^\circ\text{C}$ ) obtained by Friedel-Crafts reaction of

anisole with isocaproyl chloride, was converted into IIIb by Grignard reaction with methylmagnesium bromide, and then IIIb was dehydrated by boiling with acetic anhydride to the unsaturated phenol ether IV (b. p.  $109\sim 115^\circ\text{C}/1\text{ mmHg}$ ).



Catalytic hydrogenation of IV gave Va (b. p.  $107\sim 113^\circ\text{C}/1\text{ mmHg}$ ), which was hydrolyzed by boiling with hydroiodic acid in acetic acid to afford the phenol Vb (b. p.  $127\sim 128^\circ\text{C}/1\text{ mmHg}$ ). High pressure catalytic hydrogenation of Vb (Raney nickel, 130 atms.,  $30^\circ\text{C}$ ) yielded the alcohol VIa (b. p.  $120\sim 121^\circ\text{C}/1\text{ mmHg}$ ), which was oxidized with potassium dichromate in sulfuric acid to the ketone VIb (b. p.  $113\sim 114^\circ\text{C}/1\text{ mmHg}$ ; semicarbazone, m. p.  $149\sim 150^\circ\text{C}$ ). The cyanohydrin acetate VII (b. p.  $145\sim 147^\circ\text{C}/1\text{ mmHg}$ ) prepared from VIb with potassium cyanide and acetic anhydride, was pyrolyzed by passing through a heated Pyrex tube ( $600^\circ\text{C}$ ) packed with ceramic Raschig rings to give unsaturated cyanide VIIIa, which was then hydrolyzed to the unsaturated acid VIIIb (b. p.  $163\sim 165^\circ\text{C}/1\text{ mmHg}$ ).



Although two racemic forms are expected for the structure VIIIb, the infrared absorption spectrum of synthetic VIIIb was found superimposable on that of (+)-desoxo-todomatuic acid (Ib) (m. p.  $59\sim 60^\circ\text{C}$ ,  $[\alpha]_D^{27} + 94.3^\circ$  in ethanol; anilide, m. p.  $78\sim 79^\circ\text{C}$ ) obtained by Wolff-Kishner reduction of Ia. Catalytic hydrogenation of the methyl ester Ic of natural Ib gave saturated methyl ester IXb in which only one asymmetric center remains.

Heating with sodium methoxide converted IXb into more stable methyl ester Xa, which was hydrolyzed to give (+)-dihydro-desoxo-todomatuic acid (Xb) (b. p.  $150\sim 153^\circ\text{C}/1\text{ mmHg}$ ,  $n_D^{18} 1.4723$ ,  $[\alpha]_D^{27} + 14.1^\circ$  in ethanol; anilide Xc, m. p.  $115\sim 116^\circ\text{C}$ ). Following the same procedure, racemic IXb gave (±)-dihydro-desoxo-todomatuic acid (Xb) (b. p.  $152\sim 155^\circ\text{C}/1\text{ mmHg}$ ,  $n_D^{18} 1.4723$ ; anilide, Xc

1) R. Tuchihasi and T. Hanzawa, *J. Chem. Soc. Japan, Pure Chem. Sec. (Nippon Kagaku Zasshi)*, **61**, 1041 (1940).

2) T. Momose, *J. Pharm. Soc. Japan (Yakugaku Zasshi)*, **61**, 288 (1941).

m. p. 105~106°C). The infrared absorption spectra of racemic Xb, Xc and natural Xb, Xc were found superimposable in every detail.

These findings firmly establish the structure of todomatuic acid.

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