

# Usnic Acid. XV. Alkaline Degradation of Usnic Acid

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## Usnic Acid. XV.<sup>1)</sup> Alkaline Degradation of Usnic Acid

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The alkaline degradation product of usnic acid was identified as 4,6-dihydroxy-3,5-dimethylcoumaran-2-one on the basis of spectral and chemical evidence. The reaction mechanism is discussed.

**Keywords**—usnic acid; alkaline degradation; 4,6-dihydroxy-3,5-dimethylcoumaran-2-one; <sup>13</sup>C-NMR; <sup>1</sup>H-NMR; reaction mechanism

Some reports have appeared on the alkaline degradation products of usnic acid in a hydrogen stream, indicating them to be benzofuran-type compounds, such as usnetic and decarbousnic acids.<sup>3)</sup> This paper deals with a new alkaline degradation product of usnic acid in an oxygen stream. Usnic acid was hydrolyzed with 50% (w/v) sodium hydroxide solution in an oxygen stream and the hydrolysate was treated as mentioned in "Experimental" to afford colorless needles, C<sub>10</sub>H<sub>10</sub>O<sub>4</sub> (I), of mp 162°. Compound I shows ultraviolet (UV) absorption maxima at 210 nm (log ε 4.10, an end absorption), 278 nm (log ε 3.33) and 283 nm (log ε 3.33) and infrared (IR) absorption bands (cm<sup>-1</sup>) at 3400 (OH), 1765 (β,γ-unsaturated γ-lactone), 1640 and 1530 (benzene ring), but it does not show IR bands at 1690 (α,β,γ,δ-unsaturated C=O) or 1540 (broad, characteristic of a triketone),<sup>4)</sup> which are observed in the IR spectrum of usnic acid, suggesting that ring B of usnic acid was decomposed. Compound I was positive to the Gibbs test. On methylation with diazomethane, I afforded colorless needles of dimethyl ether, C<sub>12</sub>H<sub>14</sub>O<sub>4</sub> (II), of mp 122°, which showed IR bands at 1790 (β,γ-unsaturated γ-lactone), 1620, 1510 (benzene ring) and showed no OH band. Compound II gave proton magnetic resonance (<sup>1</sup>H-NMR) signals (δ-value, ppm in CDCl<sub>3</sub>) at 1.54 (d, 3H, J=7.5 Hz), 3.71 (q, 1H, J=7.5 Hz), assignable to a CH<sub>3</sub>-CH< group, at 2.08 (s, 3H, an aromatic-CH<sub>3</sub> group), at 3.85 (s, 6H, two O-methyl groups) and at 6.20 (s, 1H, an aromatic proton). Compound I was proved to be identical with the compound obtained by hydrolysis of the ozonolysis product (III)<sup>3)</sup> of diacetylusnic acid under the conditions described above, by mixed fusion and IR spectroscopy. This hydrolysate was identified as the desacetyl derivative of 7-acetyl-4,6-dihydroxy-3,5-dimethylcoumaran-2-one<sup>3)</sup> on the basis of the spectral and chemical properties. These findings indicate that compound I is 4,6-dihydroxy-3,5-dimethylcoumaran-2-one (Chart 1). The <sup>13</sup>C-NMR spectrum of II could be interpreted as shown in Table I.

Compound I was also obtained from usnic acid by hydrolysis in a nitrogen stream, but was not obtained from usnetic acid by hydrolysis in an oxygen stream.

The mechanism of the formation of I from usnic acid by hydrolysis in an oxygen stream or in a nitrogen stream was tentatively considered to be as shown in chart 1. Usnic acid, when attacked by OH<sup>-</sup> at the C<sub>4a</sub> carbon (the Michael reaction), might be converted to an intermediate (A⇌A'), which might be further converted to intermediate B by retro-Aldol

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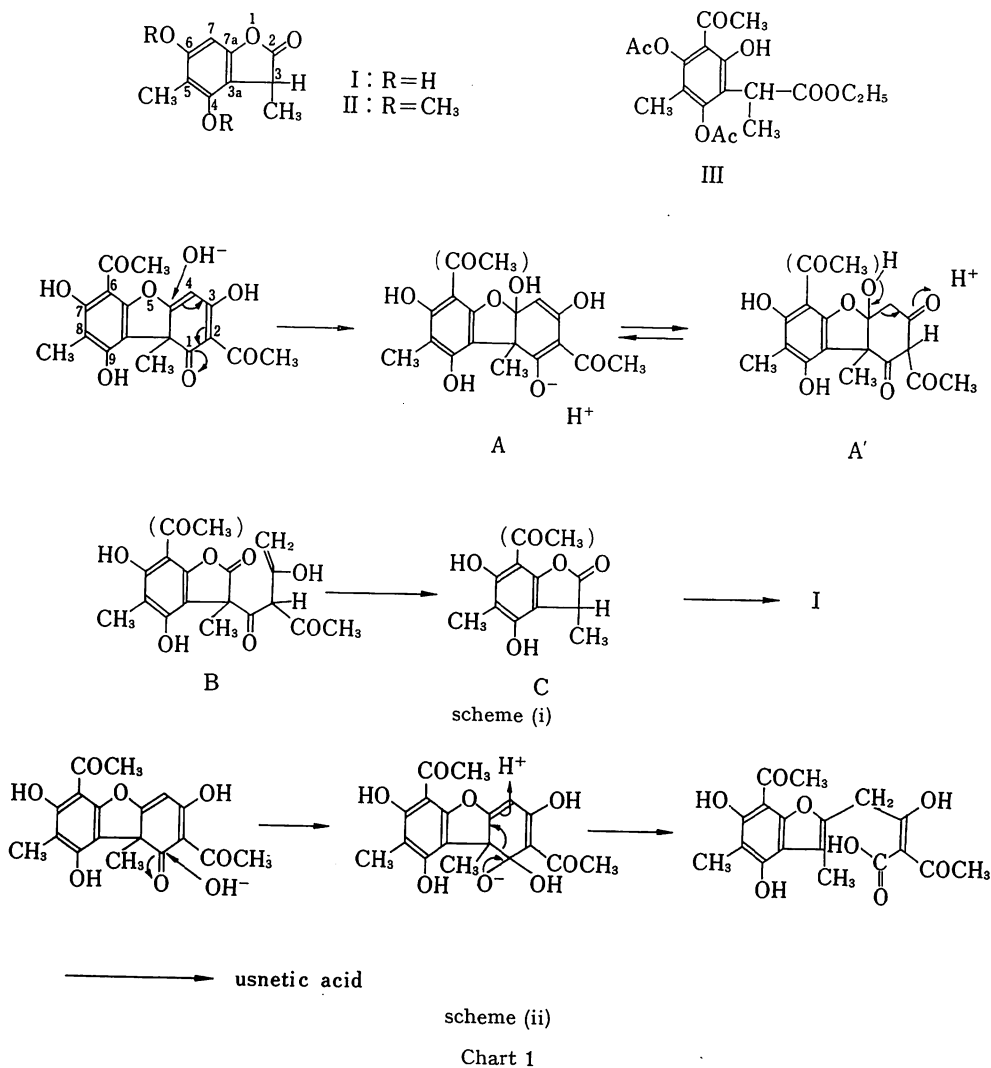


TABLE I. NMR Data for II ( $\delta$ -Values in  $\text{CDCl}_3$ , 25.15 MHz,  $J$  in Hz)

	Chemical Shift <sup>a)</sup>	Multiplicity	$J^b)$
$\text{C}_5\text{-CH}_3$	8.1	q	$J_{\text{C-H}} = 128$
$\text{C}_3\text{-CH}_3$	15.3	q, d	$J_{\text{C-H}} = 131$ , $J_{\text{CH}_3\text{-C}_1\text{H}} = 6$
$\text{C}_3$	37.9	d, q	$J_{\text{C}_1\text{-H}} = 135$ , $J_{\text{C}_1\text{-C}_3\text{CH}_3} = 5$
$\text{C}_7$	90.7	d	$J_{\text{C}_1\text{-H}} = 156$
$\text{C}_5$	102.7	q, d	$J_{\text{C}_1\text{-C}_5\text{CH}_3} = 6$ , $J_{\text{C}_1\text{-C}_7\text{H}} = 6$
$\text{C}_{3a}$	107.3	d, d	$J_{\text{C}_1\text{-C}_3\text{H}} = 5$ , $J_{\text{C}_1\text{-C}_3\text{CH}_3} = 9$
$\text{C}_4$	152.9	q, d	$J_{\text{C}_1\text{-C}_4\text{CH}_3} = 4$ , $J_{\text{C}_1\text{-C}_4\text{H}} = 4$
$\text{C}_{7a}$	154.3	broad	
$\text{C}_6$	159.1	q	$J_{\text{C}_1\text{-C}_6\text{CH}_3} = 4$
$\text{C}_2$	178.7	d, q	$J_{\text{C}_1\text{-C}_2\text{H}} = 5$ , $J_{\text{C}_1\text{-C}_2\text{CH}_3} = 6$
$\text{OCH}_3$	55.5	q	$J_{\text{C-H}} = 144$
	55.9	q	$J_{\text{C-H}} = 144$

<sup>a)</sup> ppm relative to TMS, measured with complete decoupling.

<sup>b)</sup> Measured without decoupling and assigned tentatively.  
Digital resolution was 1.2 Hz.

transformation, and intermediate B might then be converted to compound I by ketonic fission. The reaction probably does not involve auto-oxidation. On the other hand, usnic acid, when attacked by  $\text{OH}^-$  at its  $\text{C}_1$  carbon, might be converted to usnetic acid, as shown by scheme (ii) in Chart 1.

Coumaran-2-one compounds of the phloroglucinol type have been obtained from diacetyl-usnic acid by ozonolysis<sup>3)</sup> and also from diacetyldihydrousnic acid<sup>5)</sup> and diacetyltetrahydro-desoxyusnic acid<sup>6)</sup> by pyrolysis in the absence of calcium chloride, and coumaran-2-one compounds of the resorcinol type have been obtained from dihydrousnic acid and tetrahydro-desoxyusnic acid by pyrolysis in the presence of calcium chloride.<sup>7)</sup> The authors have already reported<sup>6,7)</sup> on the mechanism of the pyrolysis of dihydrousnic acid and tetrahydrodesoxy-usnic acid. It is interesting that compound I, of coumaran-2-one type, is obtained from usnic acid by hydrolysis, in addition to usnetic acid and pyrousnic acid.

### Experimental

The following instruments were used for determining physical data. Melting point: Yanagimoto micro-melting apparatus (a hot plate type); UV spectra (in EtOH): Hitachi 323 recording spectrometer; IR spectra (in KBr,  $\text{cm}^{-1}$ ): Nippon Bunko IR-G spectrometer;  $^1\text{H-NMR}$ : JNM-FX-100S instrument at 100 MHz ( $^{13}\text{C-NMR}$  at 25.15 MHz), with  $(\text{CH}_3)_4\text{Si}$  as an internal standard; mass spectra (MS): JMS-01SG spectrometer (direct inlet, with an ionizing current of 200  $\mu\text{A}$ , ionizing energy of 75 eV and source temperature of 95°); thin-layer chromatography (TLC) was carried out on glass plates coated with silica gel G (Merck) and column chromatography with silica gel (Merck), unless otherwise stated. Abbreviations: s: singlet, d: doublet, t: triplet, q: quartet m: multiplet.

**Hydrolysis of Usnic Acid in an Oxygen Stream**—Usnic acid (7.2 g) in 50% (w/v) sodium hydroxide solution (45 ml) was hydrolyzed in an oxygen stream on a boiling water bath for 1 hr, then the reaction mixture was poured into ice-water and acidified with conc. HCl to afford a precipitate, which contained usnetic acid ( $R_f=0.33$ , TLC, silica gel, impregnated with 0.1 N  $(\text{COOH})_2$ ,  $\text{CHCl}_3$ -acetone=10:1) and pyrousnic acid ( $R_f=0.05$ , TLC, silica gel impregnated with 0.1 N  $(\text{COOH})_2$ ,  $\text{CHCl}_3$ -acetone=10:1) were detected. The acidic aqueous layer was extracted thoroughly with ethyl acetate and the ethyl acetate layer was concentrated *in vacuo*, after washing with water then drying with sodium sulfate, to afford an oily substance. This was column chromatographed twice on silica gel with ethyl acetate- $\text{CHCl}_3$  (1:1) and the fraction of  $R_f$  0.62 (TLC, ethyl acetate- $\text{CHCl}_3=1:1$ ) (oil 0.85 g) was chromatographed on silica gel (100 g) with acetone- $\text{CHCl}_3$  (1:5). The fraction of  $R_f$  0.32 (TLC, silica gel acetone- $\text{CHCl}_3=1:5$ ) afforded a powder, which was purified by sublimation *in vacuo* at 130° to afford colorless needles (I) of mp 162°. (Yield: 0.36 g).  $[\alpha]_{\text{D}}^{25}=0^\circ$  ( $c=1.00$ , MeOH). The  $R_f$  values of I and the powder were the same. *Anal.* Calcd for  $\text{C}_{10}\text{H}_{10}\text{O}_4$ : C, 61.85; H, 5.19. Found: C, 61.66; H, 5.09.  $^1\text{H-NMR}$  ( $\delta$ -value in  $\text{C}_6\text{D}_6\text{N}$ , 60 MHz): 1.67 (d, 3H,  $J=7.3$  Hz,  $\text{C}_3$ - $\text{CH}_3$ ), 2.35 (s, 3H,  $\text{C}_5$ - $\text{CH}_3$ ), 3.98 (q, 1H,  $J=7.3$  Hz,  $\text{C}_3$ -H), 6.35 (s, 1H,  $\text{C}_7$ -H), 11.33 (s, 2H,  $\text{C}_4$ -OH and  $\text{C}_6$ -OH). MS ( $m/e$ , relative intensity): 194 ( $\text{M}^+$ , 64.5), 179 ( $\text{M}^+-\text{CH}_3$ , 6.3), 166 ( $\text{M}^+-\text{CO}$ , 100), 165 ( $m/e$  166-H, 17), 151 ( $m/e$  166- $\text{CH}_3$ , 25), 138 ( $m/e$  166-CO, 8), 123 ( $m/e$  138- $\text{CH}_3$ , 15). IR ( $\text{cm}^{-1}$ ): 3400, 1765, 1640, 1530, 1470, 1430, 1370, 1240, 1220, 1165, 1080, 1060, 1020, 825. Gibbs test: red-violet in the Clark and Lubs buffer solution (boric acid-KCl-NaOH, pH=9.4).

**Methylation of I**—Compound I (300 mg) in MeOH was methylated with excess diazomethane in ether for 3 days. The crude methylate was chromatographed on silica gel with  $\text{CHCl}_3$ -benzene (1:1) and the fraction of  $R_f$  0.67 (TLC,  $\text{CHCl}_3$ -benzene=1:1) afforded a colorless substance, which was crystallized from ethanol to afford the methylate (II), as colorless needles of mp 122°. *Anal.* Calcd for  $\text{C}_{12}\text{H}_{14}\text{O}_4$ : C, 64.85; H, 6.35. Found: C, 64.83; H, 6.34.

**Alkaline Degradation of III in an Oxygen Stream**—Compound III (2 g) in 50% (w/v) NaOH solution (12 ml) was hydrolyzed in an oxygen stream on a boiling water bath for 1 hr. The reaction mixture was poured into ice-water, acidified with conc. HCl and extracted with ethyl acetate. The extract afforded an oily substance (0.3 g), which was chromatographed on silica gel (40 g) with acetone- $\text{CHCl}_3$  (1:5). The fraction of  $R_f$  0.32 (TLC, acetone- $\text{CHCl}_3=1:5$ ) (powder, 235 mg) was purified by sublimation *in vacuo* at 130° to afford colorless needles of mp 162°, which were proved to be identical with compound I by mixed fusion and IR. *Anal.* Calcd for  $\text{C}_{10}\text{H}_{10}\text{O}_4$ : C, 61.85; H, 5.19. Found: C, 61.56; H, 5.05. IR: 3400, 1765, 1645, 1530, 1470, 1430, 1370, 1240, 1220, 1165, 1125, 1080, 1060, 1020, 825.

**Alkaline Degradation of Usnic Acid in a Nitrogen Stream**—Usnic acid (7.2 g) in 50% (w/v) NaOH solution (44 ml) was hydrolyzed in a nitrogen stream on a boiling water bath for 1 hr. The reaction mixture

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7) K. Takahashi and M. Takani, *Chem. Pharm. Bull.*, **19**, 2079 (1971).

was treated as described for the hydrolysis of usnic acid in an oxygen stream. The ethyl acetate-soluble fraction (3.27 g) was chromatographed on silica gel with ethyl acetate- $\text{CHCl}_3$  (1:1) and the fraction of  $R_f$  0.62 (TLC, ethyl acetate- $\text{CHCl}_3$ =1:1) (0.94 g) was again chromatographed on silica gel with acetone-*n*-hexane (1:1). The fraction of  $R_f$  0.64 (TLC, acetone-*n*-hexane=1:1) (0.63 g) was further chromatographed on silica gel with  $\text{CHCl}_3$ -acetone (5:1) and the fraction of  $R_f$  0.32 (TLC,  $\text{CHCl}_3$ -acetone=5:1) (0.37 g) afforded colorless needles of mp  $162^\circ$ , after sublimation at  $130^\circ$  *in vacuo* (3 mmHg); these were identical with compound I (mixed fusion, IR, and  $R_f$  value).

**Alkaline Degradation of Usnetic Acid in an Oxygen Stream**—Usnetic acid (1.5 g) in 50% (w/v) NaOH solution was hydrolyzed on a boiling water bath for 1 hr. The reaction mixture was poured into ice-water and acidified to afford a precipitate (0.5 g), from which usnetic acid was recovered ( $R_f$  0.33, TLC, silica gel impregnated with 0.1 N  $(\text{COOH})_2$ , acetone- $\text{CHCl}_3$ =1:10). The filtrate was extracted with ethyl acetate and the ethyl acetate layer showed spots at  $R_f$  0.33 and  $R_f$  0.05 on TLC, which could be assigned to usnetic acid and pyrousnic acid, respectively; no spot assignable to I ( $R_f$  0.26, TLC, silica gel impregnated with 0.1 N  $(\text{COOH})_2$ , acetone- $\text{CHCl}_3$ =1:10) was detected.

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