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Usnic Acid. XIII.[1] The Pyrolysis of the Oxidation Product of Dihydrousnic Acid

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The structure of the degradation product of dihydrousnic acid, obtained by the oxidation with potassium permanganate, followed by the dry distillation was studied and a possible formula was put forward on basis of the chemical and spectral evidences.

Keywords——dihydrousnic acid; oxidation; pyrolysis; PMR; ^{13}C-NMR

Attention has been drawn to the remarkable differences[3] of behaviors in the degradation reactions observed between usnic- and dihydrousnic-acids. The authors have reported on the mechanism[4] of the formation of a resorcinol type of compound, 7-acetyl-6-hydroxy-3,5-dimethylcoumaran-2-one from dihydrousnic acid by the pyrolysis, and on the mechanism[1] of the formation of 3-acetyl-5-methyl-cyclopentane-1,2,4-trione, α-acetyl-γ-methyltetronic acid, 2,6-dihydroxy-3-methylacetophenone and 5-chloro-2,6-dihydroxy-3-methyl-acetophenone from dihydrousnic acid by the potassium permanganate oxidation. It should be noted that even now, the structure of the degradation product[5] of dihydrousnic acid by the potassium permanganate oxidation, followed by the dry distillation, has not been elucidated. This paper concerns the structural elucidation of the degradation product.

Dihydrousnic acid was oxidised with alkaline potassium permanganate and the reaction mixture was acidified and filtered. The chloroform-soluble fraction of the filtrate was distilled *in vacuo* to afford $C_{17}H_{18}O_5$ (I), yellow prisms of mp 219°. The fraction itself did not show the spot of I on the thin-layer chromatogram (TLC). The ultraviolet (UV) spectrum of I shows the absorption maxima (nm, log ε) at 239.5 (4.36), 287 (4.27) and 365 (3.72) and infrared (IR) bands (cm^{-1}) at 1630 (chelated $ArCOCH_3$), 1600, 1475 (benzene ring), 1210 (phenolic OH), 1150 (–C–O–C–) and 950 (isolated aromatic proton). As in the case of the previously reported compound II,[6] compound I gave a bisoxime monoanhydride $C_{17}H_{18}N_2O_4$ (III), yellow prisms of mp 249° and a monooxime anhydride $C_{17}H_{17}NO_4$ (IV), yellow prisms of mp 195°, both of which gave green coloration with $FeCl_3$. The UV spectra of I and III were respectively similar to those of II and of the corresponding bisoxime monoanhydride (V)[6] with its UV maxima at 242 (4.23), 270.5 (4.12), 278 (4.12), 289 (3.94, sh) and 332 (3.66). The compound III was oxidised with hydrogen peroxide to afford 3,5-dimethyl-4-isooxazole carboxylic acid[7] of mp 145°, suggesting that I, as II, has a $=\dot{C}-CH(COCH_3)_2$ group in its molecule. In the ^{1}H-nuclear magnetic resonance (NMR) spectrum (δ-value, ppm), the aromatic proton signal of I occurred at δ 7.21, whereas that of II at δ 7.46. The upfield shift observed for the aromatic proton of I is probably due to the anisotropic effect of the dicarbonyl

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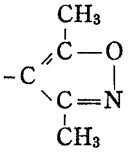
side chain which is in the form of a chelated enol and whose double bonds are in close proximity to the aromatic proton. The methyl group of I at δ 2.33, assignable to the methyl protons of the furan moiety, resonates in the lower magnetic field than that of II at δ 2.12. The δ value of the methyl signal (s, 6H) of the $=\dot{C}-CH(COCH_3)_2$ group is also different from that of the corresponding signal of II. The other signals of I are similar to the corresponding signals of II. These spectral and chemical properties suggest that I and II are isomer due to the difference in the location of the two substituents in the furan moiety. Thus, the ^{1}H–NMR spectra of I, III and IV could be interpreted as shown in Table I, taking the ^{1}H–NMR spectra of II, V and monoxime anhydride (VI)[6] of II into consideration. To

Table I. The ^{1}H–NMR Data (100 MHz in $CDCl_3$, J in Hz)

	Shieldings						
		Furan-CH_3	CH-$(COCH_3)_2$	Ar-CH_3	$ArCOCH_3$ (CH_3 / C=NOH)	Ar-H	OH: Chelated (Non chelated)	OH: Enol-chelated
I		2.33 s, 3H	1.92 s, 6H	2.26 d, 3H J=0.4	2.89 s, 3H	7.21 Dull 1H	13.05 s, 1H	16.82 s, 1H
II		2.12 s, 3H	2.04 s, 6H	2.33 d, 3H J=0.8	2.85 s, 3H	7.46 Dull 1H	13.07 s, 1H	16.72 s, 1H
III	2.10, 2.24, 2.25 Each, s, 3H			2.22 d, 3H J=0.8	(2.65 s, 3H)	6.94 Dull 1H	(7.95 Broad)	
IV	2.16, 2.31, 2.36 Each, s, 3H			2.27 d, 3H J=0.8	2.92 s, 3H	7.15 Dull 1H	13.10 s, 1H	
V	2.15, 2.33, 2.43 Each, s, 3H			2.37 d, 3H J=0.8	(2.66 s, 3H)	7.26[a] Dull 1H	(8.56 Broad)	
VI	2.15, 2.31, 2.43 Each, s, 3H			2.34 d, 3H J=0.8	2.86 s, 3H	7.49 Dull 1H	13.15 s, 1H	

a) This signal was observed at δ 7.18 in a CCl_4 solution.
Abbreviations: s, singlet; d, doublet.

interpret the ^{13}C–NMR spectrum of I, the ^{13}C–NMR spectrum of II was studied all signals (δ value, ppm) of II could be assigned to their appropriate carbons, as shown in Table II, taking into consideration the ^{13}C–NMR spectra of benzofuran,[8] the pyrolysis product (VII)[6] of tetrahydrodesoxyusnic acid, usnetol (VIII),[3] ethyl acetousnetate (IX),[3] 4-O-methyl methyl usnetate (X)[3] and the additivity effects of substituents.[9] The ^{13}C–NMR spectrum of I bears a close resemblance to that of II, except some signals. Especially, the δ values of the signals of the benzene carbons, the carbons of the $ArCOCH_3$ group and the aromatic methyl carbon of I are almost equal to those of the corresponding carbons of II, respectively. The δ values of the signals of the C_3- carbon and of the carbon of the enolated $CH(COCH_3)_2$ group of I were slightly different from those of the corresponding carbons of II, respectively. Compounds I and II exhibit respectively a signal of a methyl carbon at δ 8.5 and at δ 12.4. The former and the latter values are respectively nearly equal to those of the methyl carbons at the C_3 and at the C_2 of 2,3-dimethylbenzofuran[8] and VIII. This spectral evidence supports that I and II are isomer due to the difference in the location of the two substituents in the furan

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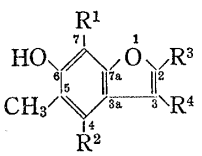
9) J.B. Stothers, "Carbon-13 NMR Spectroscopy," Academic Press, 1972, p. 95, 97, 197 and 215.

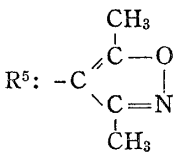
TABLE II. The ^{13}C-NMR Data (δ-Value in $CDCl_3$, 25.15 MHz) (Complete Decoupling)

Carbon	Shieldings[a] I	II	VII	VIII[b]	IX[b]	X
C_2–$\underline{C}H_3$	12.4(q)			11.3(q)		
C_3–$\underline{C}H_3$		8.5(q)	7.9(q)	7.7(q)	7.6(q)	8.3(q)
C_5–$\underline{C}H_3$	16.3(q)	16.1(q)	16.1(q)	9.8(q)	9.8(q)	9.1(q)
$CH(CO\underline{C}H_3)_2$	23.8(q)	23.8(q)				
$ArCO\underline{C}H_3$	32.0(q)	32.0(q)	31.8(q)	30.8(q)	31.4(q)	31.3(q)
$\underline{C}H(COCH_3)_2$	102.2(s)	103.9(s)				
C_2	151.4(s)[c]	146.6(s)	145.0(s)	148.0(s)	144.6(s)	143.9(s)
C_3	111.1(s)	114.9(s)	112.8(s)	110.4(s)	114.3(s)	112.4(s)
C_{3a}[d]	120.3(s)	120.9(s)	121.0(s)	112.3(s)	112.1(s)	115.1(s)
C_4	126.8(d)	127.4(d)	127.1(d)	156.9(s)	157.2(s)	158.5(s)
C_5[d]	122.5(s)	122.2(s)	122.0(s)	105.3(s)	105.7(s)	114.2(s)
C_6[d]	159.4(s)	160.2(s)	159.8(s)	162.5(s)	163.2(s)	162.0(s)
C_7	106.1(s)	106.1(s)	106.0(s)	102.1(s)	102.1(s)	104.1(s)
C_{7a}[d]	151.4(s)[c]	151.9(s)	151.6(s)	150.8(s)	154.4(s)	153.3(s)
$CH(\underline{C}OCH_3)_2$	192.6(s)	193.7(s)				
$Ar\underline{C}OCH_3$	203.0(s)	202.8(s)	202.8(s)	201.1(s)	201.2(s)	201.7(s)
Other carbons		CH_2	41.0(t)	CH_2	40.9(t)	CH_2 32.2(t)
		C=O	205.9(s)	C=O	198.8(s)	C=O 169.4(s)
		CH_2	43.8(t)	CH_2	48.7(t)	O
		CH_2	16.9(t)	C=O	167.5(s)	CH_3 52.4(q)
		CH_3	13.6(q)	O		
				CH_2	61.5(t)	OCH_3 61.7(q)
				CH_3	14.3(q)	

a) The letter in parentheses designates the multiplicity of the signal with off-resonance decoupling: s, singlet; d, doublet; t, triplet; q, quartet.
b) measured in CD_3COCD_3.
c) These signals could be considered to be overlapped with each other.
d) The signal height of the C_5 and the C_6 carbons are respectively assumed to be larger than those of the C_{3a} and C_{7a} carbons.

moiety, as mentioned above. Accordingly, the ^{13}C-NMR spectrum of I could be interpreted as shown in Table II. When benzofuran was chosen as a standard compound,[8] the shielding values of the carbons of I, II, VII, VIII, IX and X were respectively nearly similar to their calculated values.[9] The mass (MS) spectrum of I was similar to that of II, although the intensities of some peaks of I were not always equal to those of the corresponding peaks of II.





	R^1	R^2	R^3	R^4
I	$COCH_3$	H	CH_3	$CH(COCH_3)_2$
II	$COCH_3$	H	$CH(COCH_3)_2$	CH_3
III	$C(CH_3)$=NOH	H	CH_3	R^5
IV	$COCH_3$	H	CH_3	R^5
V	$C(CH_3)$=NOH	H	R^5	CH_3
VI	$COCH_3$	H	R^5	CH_3
VII	$COCH_3$	H	$CH_2COCH_2CH_2CH_3$	CH_3
VIII	$COCH_3$	OH	CH_3	CH_3
IX	$COCH_3$	OH	CH_2COCH_2COOEt	CH_3
X	$COCH_3$	OCH_3	CH_2COOCH_3	CH_3

Chart 1

On basis of these spectral and chemical evidences, the structure (I) was proposed for the degradation product, as shown in Chart 1. Studies on the mechanism of the formation of I from dihydrousnic acid are now in progress.

Experimental

Melting points were taken on a Kofler type hot plate and uncorrected. The IR spectra were taken in KBr pellet with Nippon Bunko IR-G spectrometer, the ^{1}H-NMR spectra in $CDCl_3$ and the ^{13}C-NMR spectra in $CDCl_3$ or CD_3-CO-CD_3 with JNM-PS-100 high resolution instrument at 100 MHz and at 25.15 MHz, respectively with $(CH_3)_4Si$ as internal reference, MS spectra with JMS-O1G mass spectrometer and the UV spectra with Hitachi 323 recording spectrometer in ethanol. The TLC was performed on Silica gel G (Merck) and Silica gel and Silicic acid (Mallinckrodt) were used for the column chromatography.

Oxidation, followed by Dry Distillation of Dihydrousnic Acid——A solution of 3.2 g of dihydrousnic acid in 40 ml of 10% KOH was diluted to 1 l with water. To this solution, 100 ml of 4% $KMnO_4$ was added in drops during 4 hr under vigorous stirring at room temperature. The filtered solution was acidified with dil. HCl and then filtered. The filtrate was salted out with NaCl and extracted with $CHCl_3$ several times. From $CHCl_3$ solution, 3-acetyl-5-methylcyclopentane-1,2,4-trione, α-acetyl-γ-methyl tetronic acid, 2,6-dihydroxy-3-methyl-acetophenone and 5-chloro-2,6-dihydroxy-3-methylacetophenone have been isolated.[1] The $CHCl_3$ solution was evaporated to dryness to afford an oil, which was, without purification, distilled at 150—230° (bath temperature) under 1 mmHg pressure. From 32 g of dihydrousnic acid was obtained 2 g of the distillate, which was chromatographed on silica gel (300 g) with benzene–acetone (50: 1). The fraction of *Rf* 0.22 (TLC, benzene) was crystallised from benzene–methanol to afford the compound I (80 mg), yellow prisms of mp 219°. (lit.[5] mp 217°). $FeCl_3$ reaction: red brown. *Anal.* Calcd. for $C_{17}H_{18}O_5$: C, 67.54; H, 6.00. Found: C, 67.41; H, 6.01. The fraction of *Rf* 0.14 afforded 1.3 g of methylresacetophenone, yellow needles of mp 138°. (mixed fusion and IR).

Oximation of I——A mixture of I (200 mg), hydroxylamine–HCl (120 mg), pyridine (0.2 ml) and ethanol (4 ml) was refluxed on a steam bath for 5 hr. The reaction mixture was evaporated to dryness *in vacuo* to afford yellow powder, which was washed with 3% HCl and then water. The powder was chromatographed on a silica gel (36 g) with benzene–AcOEt (50: 1). The fraction of *Rf* 0.2 (TLC, benzene–AcOEt=50: 1) afforded bisoxime monoanhydride (III), yellow prisms of mp 249° from ethanol. Yield: 65 mg. UV λ_{max} nm (log ε): 236 (4.35), 268.5 (3.97, sh), 277 (4.03), 286 (3.94, sh), 332 (3.55), IR ν_{max} cm^{-1}: 3500, 3200, 1625, 1610, 1300, 1110, 960. *Anal.* Calcd. for $C_{17}H_{18}N_2O_4$: C, 64.95; H, 5.77; N, 8.91. Found: C, 65.06; H, 5.73; N, 9.73. The fraction of *Rf* 0.44 (TLC, benzene–AcOEt=50: 1) afforded monooxime anhydride (IV), yellow prisms of mp 195° from ethanol. Yield: 14 mg. UV λ_{max} nm (log ε): 239 (4.15), 287 (3.73), 365 (3.41). IR ν_{max} cm^{-1}: 1630 (C=O), 1610, 1325, 1115, 1020, 940. *Anal.* Calcd. for $C_{17}H_{17}NO_4$: C, 68.21; H, 5.73; N, 4.68. Found: C, 68.32; H, 5.67; N, 5.14.

Hydrogen Peroxide Oxidation of III——To a solution of III (160 mg) in 10% KOH (10 ml), 10 ml of 5% H_2O_2 was added three times at an interval of 30 min, under stirring and then the solution was warmed on a steam bath at 70° for 1 hr. After being cooled, the solution was acidified with dil. HCl and salted out with NaCl and then extracted with benzene. The benzene-soluble fraction was chromatographed on silicic acid (15 g) with benzene–acetone (10: 1). The fraction of *Rf* 0.24 (TLC, benzene–acetone=10: 1, silica gel impregnated with 0.1 N $(COOH)_2$) was sublimated at 90° under 1 mmHg pressure to afford colorless needles of mp 145°, which was proved to be identical with authentic sample of 3,5-dimethyl-4-isooxazolecarboxylic acid (lit.[7] mp 142°) by the mixed fusion and IR. IR ν_{max} (cm^{-1}): 3000 (OH), 1720 (COOH), 1600, 1120, 745. *Anal.* Calcd. for $C_6H_7NO_3$: C, 51.06; H, 5.00; N, 9.93. Found: C, 51.10; H, 4.94; N, 9.71.

MS of I and II——*m/e* and intensity. The figures in the first square blackets stand for the intensities of the ions from I and those in the second square blackets for the intensities of the corresponding ions from II. *m/e* 302 (M^+) [100] [100], *m/e* 287 (M^+-CH_3) [4] [4], *m/e* 284 (M^+-H_2O) [12] [12], *m/e* 269 (*m/e* 284—CH_3) [3] [22], *m/e* 260 ($M^+-C_2H_2O$) [54] [21], *m/e* 259 (M^+-COCH_3) [15] [58], *m/e* 242 (*m/e* 284$-C_2H_2O$) [10] [11], *m/e* 241 (*m/e* 284$-COCH_3$) [13] [30], *m/e* 227 (*m/e* 242$-CH_3$) [2] [2], *m/e* 218 (*m/e* 260$-C_2H_2O$) [19] [14], *m/e* 217 (*m/e* 260$-COCH_3$) [6] [4], *m/e* 205 [6] [2], *m/e* 203 (*m/e* 218$-CH_3$) [2] [2], *m/e* 176 (*m/e* 218$-C_2H_2O$) [7] [1], *m/e* 175 (*m/e* 218$-COCH_3$) [6] [4].

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