Chem. Pharm. Bull. 26(11)3585—3587(1978)

UDC 547.728.2.04 : 541.144.04

Usnic Acid. XIV.[1] The Photo-Oxidation of Usnic Acid

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(Received May 24, 1978)

Irradiation of *d*-usnic acid at −20° under oxygen atmosphere afforded 2,4-diacetyl-6-methyl-phloroglucinol (IV), together with racemic usnic acid, and decarbousnic acid afforded also the same compound under the same conditions. The mechanism of the photo-oxidation of usnic- and decarbousnic-acids was studied.

Keywords——photosensitized oxidation; usnic acid; decarbousnic acid; 2,4-diacetyl-6-methyl-phloroglucinol; PMR; mechanism

In a previous paper of this series,[3] the authors reported on the structural elucidation of photolysis products of dihydro- and methyldihydro-usnic acids and proposed the mechanism of the photolysis. While *ortho*-type cyclohexadienones undergo a facile ring fission to acids or their derivatives by irradiation (>300 nm) in the presence of a suitable nucleophile under nitrogen atmosphere,[4] *l*-usnic acid was reported to result only in racemization in dioxane.[5] This fact indicates that the fate of the ring fission products from such cyclohexadienones would be the recyclization, if a suitable nucleophile is not present in the reaction medium. This paper deals with the photo-reaction of *d*-usnic acid in the absence of nucleophile under oxygen atmosphere affording the decomposition product obviously arisen from the ring fission intermediate. *d*-Usnic acid (I) in tetrahydrofuran (THF) was irradiated by a high pressure mercury lamp at −20° in the presence of benzophenone as a sensitizer to afford colorless needles, $C_{11}H_{12}O_5$ (IV) of mp 172°, which was proved to be identical with 2,4-diacetyl-6-methyl-phloroglucinol,[6] obtained from the ozonolysis product of diacetyldecarbousnic acid, by the mixed fusion and spectral evidence. In this case, the racemization of *d*-usnic acid was observed. Even on irradiation in the absence of benzophenone under the same conditions, *d*-usnic acid still afforded the same compound (IV).[7] The racemization of *d*-usnic acid (I) as observed in the present experiment demonstrated that the oxidation of II to III is competed with the recyclization of II to the racemic isomer (I) under these conditions. The mechanism is not only consistent with the racemization mechanism of *l*-usnic acid proposed by Barton and Quinkert,[5] but also supported by the fact that decarbousnic acid (V) by irradiation under the identical photo-oxidation conditions afforded the same compound (IV). Although additional work is required for a detailed mechanistic proposal, this photo-oxidation reaction (I—IV) is most easily interpreted on the basis of an initial ring fission giving the ketene (II), followed by the oxidation by singlet oxygen (Ene reaction[8])

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[1] Part XIII: K. Takahashi and M. Takani, *Chem. Pharm. Bull.* (Tokyo), **26**, 526 (1978).

[2] Location: *13-1 Takaramachi, Kanazawa, 920, Japan.*

[3] K. Takahashi, M. Takani and A. Fukumoto, *Chem. Pharm. Bull.* (Tokyo), **22**, 115 (1974).

[4] O.L. Chapman, "Advances in Photochemistry" [Ed. by W.A. Noyes, G. Hammond and J.N. Pitts], Vol. 1, p. 345, Interscience, New York, 1963.

[5] D.H. Barton and G. Quinkert, *J. Chem. Soc.*, **1960**, 1.

[6] C. Schöpf and F. Ross, *Liebig. Ann. Chem.*, **546**, 1 (1941).

[7] Since the present photo-oxidation proceeds without any sensitizer, we consider it reasonable that *d*-usnic acid (I) and its derivative (V) act as a sensitizer for the production of singlet oxygen. Usnic acid; $\lambda_{\max}^{\mathrm{THF}}$ nm (log ε): 233.0 (4.60), 283.0 (4.47), 340 (3.91, sh), 374 (3.73, sh). Decarbousnic acid: 244.5 (4.30), 297.5 (4.21), 348.0 (3.60).

[8] "Ene reaction is a type II photo-sensitized oxygenation in which singlet oxygen adds to an olefin to give an allylic hydroperoxide being accompanied with a shift of double bond. D.R. Kearns, *Chem. Rev.*, **71**, 395 (1971); G.O. Schenck, H.D. Becker, and K.H. Schulte-Elte, *Chem. Ber.*, **96**, 509 (1963).

to the hydroperoxide (III),[9] which decomposes giving the observed product (IV). (Chart 1).[10] The remarkable difference between the photo-reactions of usnic- and dihydrousnic-acids observed in this and the previous works have demonstrated the importance of *ortho*-dienone function in the former compound.

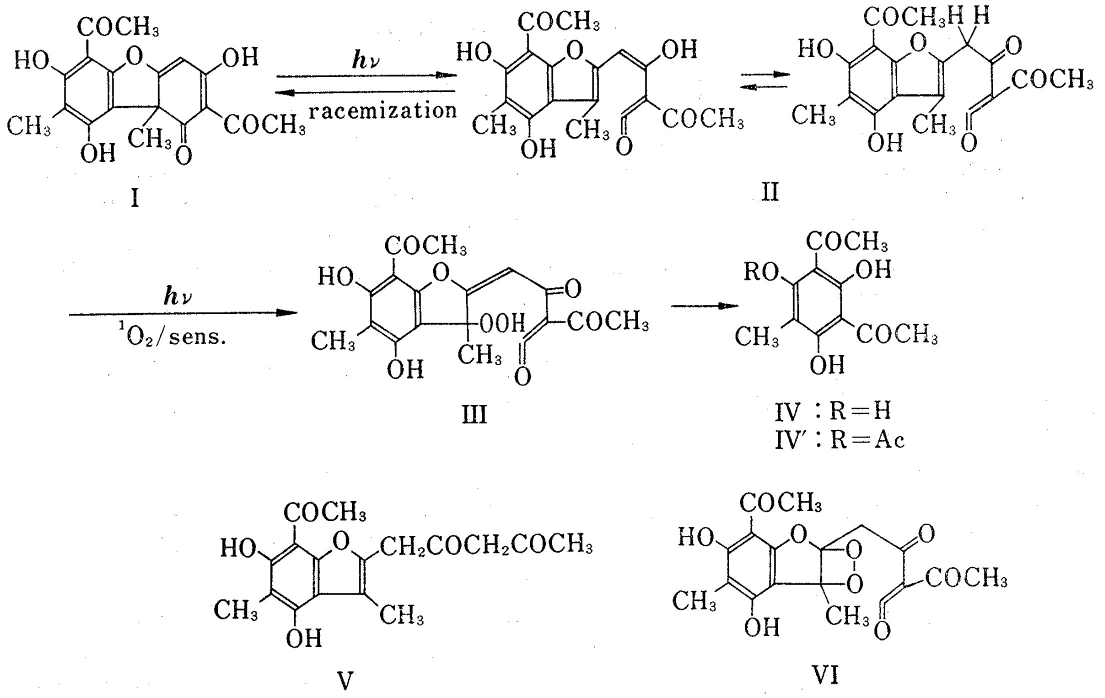

Chart 1

Experimental

Melting points were taken on a Kofler type hot plate and uncorrected. The infrared (IR) spectra were taken in KBr pellet with Nippon Bunko IR-G spectrometer, the UV spectra with a Hitachi recording spectrometer 323, the optical rotation at 589 nm with Nippon Bunko automatic polarimeter DIP-SL, the proton nuclear magnetic resonance (PMR) spectra with a JNM-PMX 60 NMR spectrometer at 60 MHz in $CDCl_3$ or C_5D_5N with $(CH_3)_4Si$ as internal reference and mass (MS) spectra with JMS-01SG mass spectrometer, the ionizing current kept at 200 μA, while ionization energy being maintained at 75 eV and source temperature at 120°. The thin-layer chromatogram (TLC) was performed on silica gel G (Merck), and silicic acid (Mallinckrodt) and silica gel (Stahl, 60) were used for the chromatography. Abbreviation: sh, shoulder; s, singlet; br, broad.

Irradiation of *d*-Usnic Acid in Tetrahydrofuran at −20°——a) *d*-Usnic acid (3.2 g) and benzophenone (103 mg) in tetrahydrofuran (560 ml) was irradiated for 15 hr at −20° under oxygen in a pyrex flask by a high pressure mercury lamp (Halos type PIH-300). The reaction mixture was then evaporated *in vacuo* to afford a resinous substance, which was treated with hot methanol (200 ml). The methanol-insoluble fraction afforded racemic usnic acid of mp 195° ($[\alpha]_D=0°$, $c=1.0$, $CHCl_3$) (1.2 g), after crystallization from benzene. The methanol-soluble fraction was column chromatographed over silicic acid (290 g) with benzene–AcOEt (10: 1). A fraction of *Rf* 0.38 (TLC, silica gel impregnated with 0.1 N $(COOH)_2$, benzene–AcOEt=10: 1) afforded pale yellow needles, which were again chromatographed over silica gel (22 g) with benzene–AcOEt (10:1) and a fraction of *Rf* 0.34 (TLC, silica gel, benzene–AcOEt=10: 1) afforded compound (IV), colorless needles of mp 172°, after crystallization from 80% methanol. Yield: 110 mg. $FeCl_3$ test: red-brown. *Anal.* Calcd. for $C_{11}H_{12}O_5$: C, 58.92; H, 5.40. Found: C, 58.64; H, 5.29. UV λ_{max}^{EtOH} nm (log ε): 274 (4.38), 295 (4.25, sh), 336 (3.68), 382 (3.42, sh). IR ν_{max}^{KBr} (cm^{-1}): 3420 (OH), 1635 (chelated C=O), 1620 (chelated

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9) While there are ample examples of the ene-reactions of indoles to give indolenine-3-hydroperoxides, precedents of the same reaction in the benzofuran derivatives are quite rare. See for example, J.J. Basselier, *Compt Rend. Acad. Sci.*, Paris, C, **273**, 514 (1971).

10) The mechanism involving the formation of the dioxetane (VI) from either II or III and its decomposition to IV can not be reagally excluded at present.

C=O), 1590 (aromatic $\nu_{C=C}$), 1490, 1440, 1360, 1270, 1190, 1130, 1100, 980, 875. PMR (δ-value in C_5D_5N): 2.28 (s, 3H, CH_3), 2.78 (s, 6H, $2\times COCH_3$), 10.53 (s, 3H, $3\times OH$). MS (*m/e*, relative intensity): 224 (68, M^+), 209 (100, M^+-CH_3), 191 (33, *m/e* $209-H_2O$), 182 (2, $M^+-C_2H_2O$), 181 (2, M^+-COCH_3), 167 (7, *m/e* $209-C_2H_2O$), 143 (3), 135 (4, *m/e* $191-CH_3\text{-}\underset{H}{C}{=}C{=}O$), 123 (5), 122 (8), 121 (8), 105 (9), 104 (14), 93 (7), 87 (10), 83 (9, *m/e* $167-CH_3CO\text{-}\underset{H}{C}{=}C{=}O$), 43 (42).

b) *d*-Usnic acid (1.2 g) in tetrahydrofuran (520 ml) was irradiated for 12 hr under oxygen at −20° without benzophenone. The reaction mixture was treated as mentioned above to afford racemic usnic acid (78 mg) and IV (100 mg) (mixed fusion). The compound (IV) was proved to be identical with 2,4-diacetyl-6-methyl-phloroglucinol[5] by the mixed fusion and UV, IR, PMR.

Ozonolysis of Diacetyl Decarbousnic Acid[6]——Diacetyl decarbousnic acid (3 g) was dissolved in CCl_4 (150 ml) and the ozonized oxygen was passed through for 4 hr at 15° and then the solvent was distilled off *in vacuo* to afford a resinous substance, which was boiled in 80% ethanol for 2 hr. After the ethanol being distilled off *in vacuo*, the remaining resinous substance was boiled in 2 N Na_2CO_3 solution for 15 min and then the solution was acidified with dil.HCl to afford a precipitate (1 g), which was chromatographed over silicic acid (100 g) with benzene–acetone (10: 1) to afford two fractions of *Rf* 0.66 (500 mg) and *Rf* 0.11 (110 mg) (TLC, silica gel impregnated with 0.1 N $(COOH)_2$, benzene–acetone=30: 1). The fraction of *Rf* 0.66 was again chromatographed over silica gel (50 g) with benzene–acetone (30: 1) and a fraction of *Rf* 0.35 (TLC, silica gel, benzene–acetone=30: 1) afforded colorless needles (IV′) of mp 120—121°, after crystallization from ethanol. Yield: 350 mg. *Anal.* Calcd. for $C_{12}H_{14}O_6$: C, 58.64; H, 5.30. Found: C, 58.62; H, 5.30. IR ν_{max}^{KBr} (cm^{-1}): 1770 (OAc), 1620 (chelated C=O), 1280, 1180, 1160, 1080, 890, 870. MS $M^+=$*m/e* 266, *m/e* 224 ($M^+-C_2H_2O$) and all species that were observed on the MS of the compound (IV). PMR (δ-value in $CDCl_3$): 1.90 (s, 3H, CH_3), 2.38 (s, 3H, $OCOCH_3$), 2.55 (s, 3H, $COCH_3$), 2.73 (s, 3H, $COCH_3$), 14.82 (s, 1H, chelated OH), 15.35 (s, 1H, chelated OH). Compound (IV′) (100 mg) was hydrolysed with conc. H_2OS_4 (1 ml) for 10 min in cold to afford 2,4-diacetyl-6-methyl-phloroglucinol (IV) of mp 172° (66 mg), after purification by the column chromatography (silica gel, benzene–AcOEt=20: 1) by the mixed fusion and IR, indicating that IV′ is 2,4-diacetyl-1-acetoxy-6-methyl-phloroglucinol. The fraction of *Rf* 0.11, mentioned above, was chromatographed over silica gel (60 g) with benzene–acetone (30: 1) and a fraction of *Rf* 0.18 (TLC, silica gel, benzene–acetone=30: 1) afforded colorless needles of mp 172°, namely 2,4-diacetyl-6-methyl-phloroglucinol (mixed fusion and IR, PMR). *Anal.* Calcd. for $C_{11}H_{12}O_5$: C, 58.92; H, 5.40. Found: C, 59.20; H, 5.30.

Irradiation of Decarbousnic Acid——a) Decarbousnic acid (1 g) in tetrahydrofuran (250 ml) was irradiated for 8 hr at −20° under oxygen. The reaction mixture was then evaporated *in vacuo* to afford a resinous substance, which was purified by the column chromatography (silica gel, benzene–AcOEt=20: 1) three times. A fraction of *Rf* 0.28 (TLC, silica gel, benzene–AcOEt=20: 1) afforded compound (IV), colorless needles of mp 172°, after crystallization from 80% methanol (mixed fusion and IR). Yield: 45 mg.

b) Decarbousnic acid (0.3 g) and benzophenone (6 mg) in tetrahydrofuran (75 ml) was irradiated for 8 hr at −20° under oxygen. The reaction mixture was then evaporated *in vacuo* to afford a resinous substance, which was chromatographed over silica gel (60 g) with benzene–AcOEt (20: 1) and a fraction of *Rf* 0.28 (TLC, silica gel, benzene–AcOEt=20: 1) afforded compound (IV), colorless needles of mp 172° (mixed fusion and IR). Yield: 10 mg.

Acknowledgement The authors express their deep gratitude to Dr. Y. Asahina (the late) for his encouragement throughout this work and to Prof. C. Kaneko of this faculty for discussing the mechanism. Thanks are due to Mr. Y. Itatani and Miss Y. Arano for elemental analyses and PMR measurement, to Miss K. Ōhata for MS, Miss Y. Hamashita and Mr. T. Matsuzaki for their technical assistances and to Mr. H. Ogata (Wako Junyaku Co., Ltd.) for supply of usnic acid.