10. **Kōtaro Takahashi:** Decomposition of Usnic Acid. IV.* A New Optically Active Product obtained by the Decomposition of Diacetylusnic Acid.

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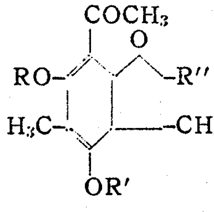
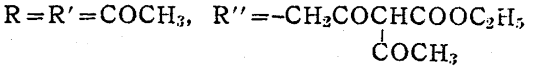
As the degradation products of usnic acid, two series of compounds, coumarone and coumaran-2-one derivatives, are known in literature. The former group includes diacetylusnic acid ethoxide (Ia), ethyl acetusnetate (Ib), decarbousnic acid (Ic), acetusnetol (Id), usnetic acid (Ie), and usnetol (If).

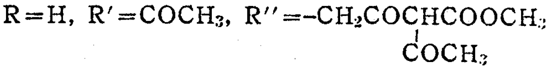
The products of ozonolysis and permanganate oxidation of diacetylusnic acid, (IIa) and (IIb), belong to the latter group.



(I a~f)



(Ia) $R=R'=COCH_3$, $R''=-CH_2CO\underset{COCH_3}{\underset{|}{C}}HCOOC_2H_5$



(Ia') $R=H$, $R'=COCH_3$, $R''=-CH_2CO\underset{COCH_3}{\underset{|}{C}}HCOOCH_3$

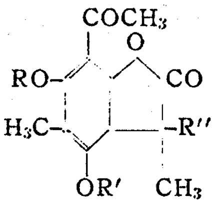
(Ib) $R=R'=H$, $R''=-CH_2COCH_2COOC_2H_5$

(Ic) $R=R'=H$, $R''=-CH_2COCH_2COCH_3$

(Id) $R=R'=H$, $R''=-CH_2COCH_3$

(Ie) $R=R'=H$, $R''=-CH_2COOH$

(If) $R=R'=H$, $R''=CH_3$



(II a~b)

(IIa) $R=R'=COCH_3$, $R''=H$

(IIa') $R=H$, $R'=COCH_3$, $R''=H$

(IIb) $R=R'=COCH_3$, $R''=COCH_3$

The discussion on the structure of usnic acid has hitherto been based on these compounds[1]. It should be noted here that no degradation products of usnic acid were obtained which retained the latter's optical activity.

The present paper is on a new type of decomposition product of usnic acid, which is noteworthy in possessing an optical activity. On treatment with 10% HCl containing methanol, diacetylusnic acid afforded a yellow-colored compound, m.p. 167~168°.

From its analytical figures, it is formulated as $C_{21}H_{22}O_9$, which would represent an addition of 1 mole of CH_3OH to monoacetylusnic acid, $C_{20}H_{18}O_8$. A methanolytic product of *d*-monoacetylusnic acid possessing the same molecular formula, $C_{21}H_{22}O_9$, was previously recorded by Asahina and Okazaki[2], from which the above-mentioned product could be differentiated by the possesstion of an optical activity.

From *d*-diacetylusnic acid, levorotatory compound, $[\alpha]_D^{10}-83.9°$, was obtained, while *l*-diacetylusnic acid yielded dextrorotatory compound, $[\alpha]_D^{10}+86.8°$, and racemic diacetylusnic acid, a corresponding optically inactive compound, m.p. 176°.

The newly obtained methanolytic product is, therefore, designated as monoacetylusnic acid isomethoxide.

Monoacetylusnic acid isomethoxide contains a methoxyl, and an O-acetyl group, and gives no coloration with *o*-phenylenediamine and Ehrlich's color reaction***. These facts ex-

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*** *p*-Dimethylaminobenzaldehyde and conc. HCl.

1) cf. Footnotes 1–3 cited in Part I of this series. (J. Pharm. Soc. Japan, **71**, 1083 (1951)).

2) Y. Asahina, K.Okazaki: J. Pharm. Soc. Japan, **63**, 618 (1943).

clude the possibility of the presence of decarbousnic acid-type of side chain and usnolic acid-type of structure.

Contrary to the parent substance, monoacetylusnic acid isomethoxide did not suffer racemization by being boiled in ethanol or xylene for many hours.

Deacetylated product, $C_{19}H_{20}O_8$, m.p. 92°, prepared from monoacetylusnic acid isomethoxide by the action of conc. H_2SO_4, yielded dicarbethoxyl derivative, $C_{25}H_{28}O_{12}$, which appeared in two crystal forms, one of m.p. 111~112° (decomp.), and the other of m.p. 101~102° (decomp.), containing 2 moles of benzene and 1 mole of toluene, respectively, depending on the solvent used for recrystallization.

The ultraviolet absorption curves of the two forms were found to be identical (Fig. 1).

On treatment with phenylhydrazine hydrochloride, monoacetylusnic acid isomethoxide gave bis(phenylhydrazone) monoanhydride, $C_{33}H_{32}O_6N_4$, m.p. 270° (decomp.).

The ultraviolet absorption curve of usnic acid isomethoxide is shown in Fig. 2 in comparison with that of methylphloroacetophenone suggesting very probably the presence of the latter structure in the molecule of the former compound.

On heating under ordinary pressure, the methanolytic product afforded a monoacetate of 7-acetyl-3,5-dimethyl-4,6-dihydroxycoumaran-2-one, m.p. 190° (II a′), liberating acetylacetone.

The same coumaran-2-one derivative was also obtained by the vacuum dry-distillation of the methanolytic product in the presence of anhydrous $CaCl_2$.

In the above case, when the decomposition was carried out under ordinary pressure, decarbousnic acid monoacetate was obtained by the subsequent vacuum distillation. Correspondingly the deacetylated product of the methanolytic product yielded decarbousnic acid by the similar treatment. Decarbousnic acid and its monoacetate were also obtained by respectively boiling usnic acid isomethoxide or its monoacetate in 95% formic acid.

Comparative study on boiling diacetylusnic acid in formic acid showed that it only suffered deacetylation.

The properties of monoacetylusnic acid isomethoxide described above have offered the following evidedce for its chemical structure: 1) Monoacetylusnic acid isomethoxide is formed from diacetylusnic acid by methanolysis and is accompanied by partial deacetylation. The asymmetric center of usnic acid nucleus is retained in the methanolytic product, but the conversion of optical properties, which, occured in this reaction, offers ground for discussions. 2) The liberation of acetylacetone by the pyrolysis and the formation of decarbousnic acid by the action of formic acid show that usnic acid isomethoxide contains a 1,3-diketone linkage.

A negative color reaction with *o*-phenylenediamine suggests that the arrangement of the ketone grouping in this compound would be the same as that in usnic acid, excluding the possibility of the presence of a straight 1,3-diketone chain as seen in decarbousnic acid. 3) Since the presence of a methoxyl was proved in bis(phenylhydrazone) monoanhydride of monoacetyl usnic acid isomethoxide, the methylation would occur in the hydroxyl other than the enol-hydroxyl of the 1,3-diketone grouping which is present in usnic acid molecule. 4) The formation of 7-acetyl-3,5-dimethyl-6-hydroxy-4-acetoxycoumaran-2-one and monoacetyl-decarbousnic acid from monoacetylusnic acid isomethoxide indicates the presence of a methylphloroacetophenone nucleus in that molecule. 5) Since the methoxyl of usnic acid isomethoxide is readily liberated forming coumaran-2-one and decarbousnic acid, it seems that the methoxyl does not exist in the phloroacetophenone nucleus.

On the basis of the above evidences, monoacetylusnic acid isomethoxide could be represented by formula (IVa), which could possibly be derived from Robertson-Schöpf's formula of usnic acid (III) by the methanolytic cleavage of the oxygen bridge.

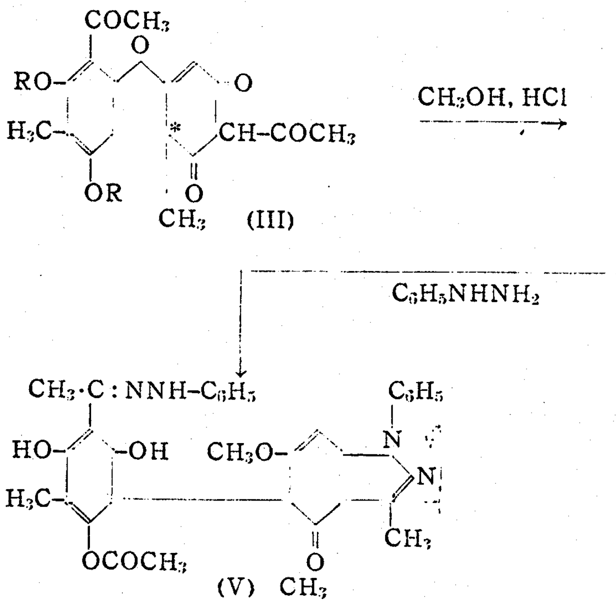


Fig. 1.

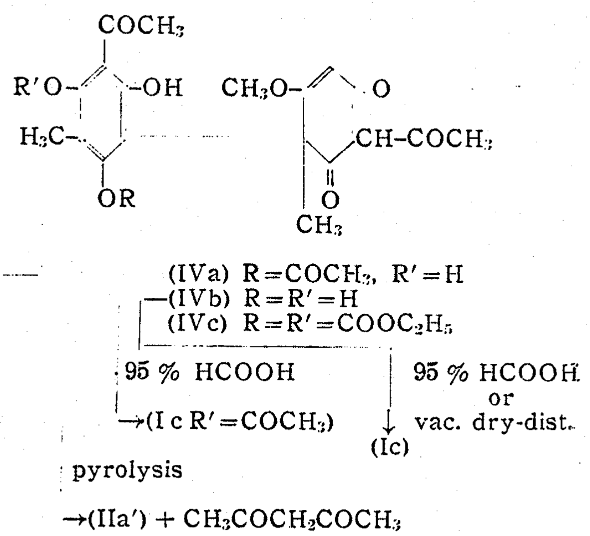
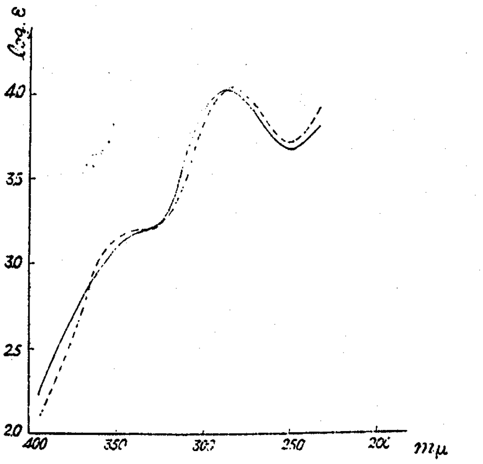
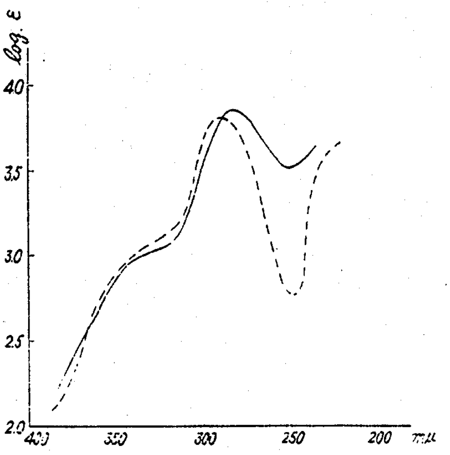


Fig. 2.



— Dicarbethoxyusnic acid isomethoxide-2C$_6$H$_5$
--- Dicarbethoxyusnic acid isomethoxide-C$_7$H$_8$
max. 284 mμ, $^1/_{20,000}$ Mol. alcoholic solution



— Usnic acid isomethoxide
max. 285 mμ, $^1/_{20,000}$ Mol. alcoholic solution
--- Methylphloroacetophenone
max. 290 mμ, $^1/_{10,000}$ Mol alcoholic solution

The author is grateful to the members of analytical laboratories of this department and the Institute of the Infectious Diseases, University of Tokyo, for the analytical determinations.

Experimental

***l*-Monoacetylusnic acid isomethoxide** — Five g. of *d*-diacetylusnic acid was boiled for 2~3 hours in 50 g. of methanol containing 10% HCl-gas. On concentration of the reaction mixture under diminished pressure, yellow crystals separated out, which were recrystallized from methanol to form yellow needles, m.p. 167~168°. Yield: 2.5~3.0 g.

The product is soluble in sodium carbonate solution, and gives a brown red coloration with ferric chloride and no coloration with *o*-phenylenediamine and Ehrlich's reagent. $[\alpha]_D^{10}$ −83.9° (c=2.980, CHCl$_3$).

Anal. Calcd for $C_{21}H_{22}O_9$: C, 60.28; H, 5.26; CH$_3$O, 7.42; CH$_3$CO, 10.28. Found: C, 60.39, 60.30, 60.46; H, 5.31 5.39, 5.24; CH$_3$O, 7.91; CH$_3$CO, 13.36.

On heating in a sealed tube with water at 150°, for 5 hours, it is almost completely recovered, accompained with a small amount of resinous substance. It also remains unchanged when boiled in 60% acetic acid for 5 hours.

By a similar treatment, *l*-diacetylusnic acid gave *d*-monoacetylusnic acid isomothoxide, $[\alpha]_D^{10}$ +68.8° (c=3.108, CHCl$_3$), m.p. 167~168°. *Anal.* Found: C, 60.05; H, 5.33.

From *dl*-diacetylusnic acid, *dl*-monoacetylusnic acid isomethoxide, m.p. 176°, was obtained. *Anal.* Found: C, 60.17; H, 5.37.

***l*-Usnic acid isomethoxide** — One g. of *l*-monoacetylusnic acid isomethoxide was dissolved in 10 cc. of conc. H_2SO_4 under ice-cooling and the mixture was poured onto ice. Yellow precipitates that separated were recrystallized from methanol to yellow needles, m.p. 92°(decomp.). $[\alpha]^{25}_{D}$ $-44.2°$ (c=2.672 $CHCl_3$).

It gives brown red coloration with ferric chloride. It gives negative color reactions with *o*-phenylenediamine and Ehrlich's reagent. *Anal.* Calcd. for $C_{19}H_{20}O_8$: C, 60.63; H, 5.30. Found: C, 60.71; H, 5.25. It contains a methoxyl.

Carbethoxylation of *l*-usnic acid isomethoxide — To a mixture of 1 g. *l*-usnic acid isomethoxide, 6 g. of dimethylaniline and 10 cc. of benzene, 3 g. of ethyl chloroformate was dropped in under ice-cooling at -10° to -15°. After 3 hours' stirring, the mixture was acidified with cold dil. HCl, and benzene layer was separated. The solvent was distilled off in vacuum to yellow needles, which were recrystallized from benzene to m.p. 111~112°(decomp.). It gives a brown red coloration with ferric chloride.

Anal. Calcd. for: $C_{25}H_{28}O_{12} \cdot 2C_6H_6$: C, 65.68; H, 5.92. Found: C, 65.75. 65.29; H, 5.73, 5.75.

The above crystals were recrystallized from toluene to yellow needles, m.p. 101–102° (decomp.).

Anal. Calcd. for $C_{25}H_{28}O_{12} \cdot C_7H_8$: C, 62.95; H, 5.8. Found: C, 63.06; H, 5.75.

bis(Phenylhydrazone) monoanhydride of *l*-monoacetylusnic acid isomethoxide — This was obtained by heating a mixture of 0.5 g. of *l*-monoacetylusnic acid isomethoxide, 0.5 g. of phenylhydrazine hydrochloride, and 0.7 g. of sodium acetate in hydrated alcohol (20 cc.) for 3 hours on a bath. Faint yellowish plates were formed by recrystallization from ethanol, m.p. 270° (decomp.).

Anal. Calcd. for $C_{33}H_{32}O_6N_4$: C, 68.27; H, 5.52; N, 9.65; CH_3O, 5.56. Found: C, 68.40, 68.42; H, 5.69, 5.58; N, 10.08; CH_3O, 6.12.

Formation of 7-acetyl-3,5-dimethyl-6-hydroxy-4-acetoxycoumaran-2-one (IIa') and monoacetyldecarbousnic acid from monoacetylusnic acid isomethoxide — On heating monoacetylusnic acid isomethoxide at 250~270° (bath temp.) under ordinary presssure, acetylacetone distilled out. After about 20 minutes' heating, the residue was distilled under a diminished pressure, when an oily substance, b.p$_3$ 240~250°, run out, which solidified on cooling.

Faint yellowish needles, m.p. 190°, were obtained by recrystallization from methanol. It gave reddish violet coloration with ferric chloride and no melting point depression on admixture with 7-acetyl-3,5-dimethyl-6-hydroxy-4-acetoxy-coumaran-2-one (m.p. 190°).

Anal. Calcd. for $C_{14}H_{14}O_6$: C, 60.43; H, 5.02. Found: C, 60.29; H, 4.84.

A mixture of 1.5 g. of monoacetylusnic acid isomethoxide and 0.7 g. of anhydrous $CaCl_2$ was distilled under diminished pressure (0.1 mm.Hg) below 240° (bath temp.), when an oily substance was obtained. After recrystallization it was proved to be identical with 7-acetyl-3,5-dimethyl-6-hydroxy-4-acetoxy-coumaran-2-one (IIa') by a mixed fusion.

One g. of monoacetylusnic acid isomethoxide was mixed thoroughly with 1 g. of anhydrous $CaCl_2$ and heated under ordinary pressure at 260~270° (bath temp.). The reaction mixture was distilled in vacuum, when an oily substance distilled at 250~260° (3 mm.Hg), which was recrystallized and proved by a mixed fusion to be identical with monoacetyldecarbousnic acid (m.p. 127°).

Formation of decarbousnic acid from *l*-usnic acid isomethoxide — A mixture of 1 g. of usnic acid isomethoxide and 1.5 g. of anhydrous $CaCl_2$ was heated at 250~260° under ordinary pressure, then distilled in vacuum (4 mm.Hg at 260~270°) by which decarbousnic acid, m.p. 174~176°, was obtained. The same result was also obtained in the absence of $CaCl_2$.

Action of 95% formic acid on *l*-usnic acid isomethoxide and its acetate — One g. of monoacetylusnic acid isomethoxide was refluxed for 1 hour in 10 cc. of 95% formic acid. The crystals that separated on cooling were recrystallized from methanol to yellow needles, m.p. 126°, which were proved by a mixed fusion to be identical with those of monoacetyldecarbousnic acid.

By a similar condition, decarbousnic acid, m.p. 176°, was obtained from usnic acid isomethoxide.

By a comparative study, boiling 1 g. of *dl*-diacetylusnic acid in 10 cc. of 95% formic acid for 1 or 3 hours, resulted in deacetylation, giving *dl*-usnic acid.

Summary

On boiling with methanol containing 10% HCl-gas, diacetylusnic acid was converted into an optically active methanolytic product formulated as $C_{21}H_{22}O_9$, which was designated as monoacetylusnic acid isomethoxide. The chemical properties and the structure of this compound were discussed and a possible formula was put forward.

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