

Some Chemical Properties of Antifungal Aldehyde from *Houttuynia cordata* Thumb.

By Yoshihisa Mizuno, Takuo Kosuge and Haruka Isogai

Introduction

Herbs of *Houttuynia cordata* Thumb (Dokudami in Japanese) was used in the treatment of inflammations and various kinds of diseases in olden times in Asia, especially in China and Japan. Dried herbs are still employed for that purpose among the country folks in that area.

A survey of the literature shows that some optically inactive carbonyl compounds of aliphatic series (*n*-capryl, *n*-lauryl aldehyde and methyl *n*-nonyl ketone) along with myrcen and quercetin have been obtained from *Houttuynia cordata* Thumb. None of them, however,

are effective enough to substantiate their claims. It is, therefore, desirable to solve the problem as to whether or not the herb actually contains effective components.

An antifungal and optically active aldehyde was found in the course of our investigation where an influence of the distillate formed by subjecting freshly ground rhizomes of the plant to steam distillation (under the diminished pressure) upon the growth of fungi was examined.

In the present paper, it is our main concern to describe some chemical properties of the new aldehyde.

Results

Needle-like crystals of comparatively low melting point (ca. 30°C) obtained from the distillate, reacted with carbonyl reagents (semicarbazide, thiosemicarbazide, *p*-nitro-phenylhydrazide and sodium bisulfite) to form semicabazone (m. p. 176-183°C under decomposition), thiosemicarbazone (m. p. 66°C), *p*-nitro-phenylhydrazone

and sodium bisulfite addition compound respectively.

The substance in question was also found to react with aldehyde reagents such as Fehling's, fuchsin, and Angeli reagent, indicating that this is an aldehyde.

Some Properties of Semicabazone, Thiosemicarbazone and Bisulfite Addition Compound of the Aldehyde.

The aldehyde was prone to be polymerized, especially in alkaline media,

making it difficult to examine the properties of the aldehyde as such,

The antifungal action of the aldehyde will be reported by H. Isogai in a separate paper.

and therefore the chemical properties of semicarbazone, thiosemicarbazone and bisulfite addition compound were examined.

The results obtained in determination of

melting point, optical activity, elementary analysis and absorption max. etc. are summarized in the following tables.

	m. p.	Optical activity	Cu-Acetate colortest	Results of assay correspond to
Semicarbazone	176–183°C		negative	$C_{13}H_{20}(=NNHCONH_2)_2 \cdot H_2O$
Thiosemicarbazone	66°C	$[\alpha]_D^{20} = -69.6$	yellowish green	$C_{13}H_{20}(=NNHCSNH_2)$
NaHSO ₃ adduct.				$C_{13}H_{21}O \cdot S \cdot O_4Na_2H_2O$

	λ max	Molecular weight
Semicarbazone	< 2500 Å	
Thiosemicarbazone		230–200

The semicarbazone failed to give positive color test both towards cupri acetate and ferri chloride, but the thio-

semicarbazone did give positive tests towards those reagents.

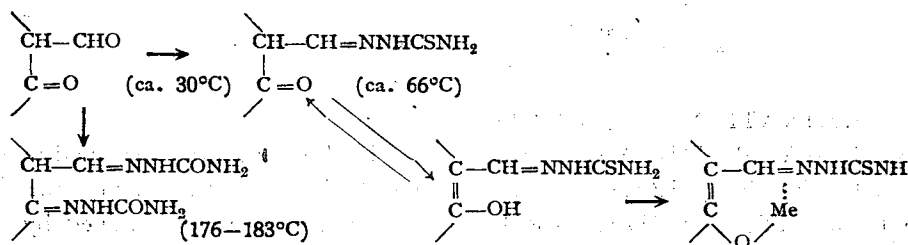
Discussion

The results obtained from assays and determination of molecular weight show that the semicarbazone and the thiosemicarbazone are bis- and monocompounds respectively.

The behavior of thiosemicarbazone toward the two ions, shows that the thiosemicarbazone molecule contains another carbonyl group which is enolisable and can afford to combine in the enolized state with ferri- and cuppi ion to form colored chelated complexes. Bissemicar-

bazone molecule, however, does not contain any enolisable carbonyl group. Such situation may be described in the following diagram.

On the basis of the result obtained by spectroscopic determination, it can be concluded that the semicarbazone does not have such a grouping as $=CH-CH=NNHCSNH_2$, because that the grouping has the absorption maxima at the wave length of 2650 Å. (c. f. Table)



Me: Fe or Cu yellowish green or greenish brown.

Experimental

PREPARATION OF MATERIALS: Rhizomes of *Houttuynia cordata* Thumb was cut into lengths of 10 cm, and the cut material was mixed with 0.1N hydrochloric acid and was ground to gruel in the mixer. The material thus treated was subjected to steam distillation under diminished pressure at the temperature of no more than 60°C. The distillate formed two layers. The whole distillate was extracted with petroleum ether and petroleum ether was

removed under reduced pressure. The residue was transformed into the semicarbazone, thiosemicarbazone and the sodium bisulfite addition compound according to the usual procedures. The semicarbazone was recrystallized several times (nine times) till the constant value of percentages of carbon, hydrogen and nitrogen could be obtained. The results obtained by assays are shown in the following table.

SEMICARBAZONE

Anal. Calcd. for $C_{15}H_{27}O_2N_7H_2O$		C: 53.57	H: 8.33	N: 25.30
Found.	C	H	N	
5	54.65	11.10	25.92	
6	53.57	8.67	26.87	
7	53.88	8.50	26.34	
8	53.77	7.32	26.11	
9	54.12	7.70	26.84	

THIOSEMICARBAZONE

Anal. Calcd. for $C_{14}H_{25}N_3S$		C: 64.2	H: 8.00	N: 15.90
Found.		C: 62.97	H: 8.31	N: 15.71

BISSULFITE ADDITION COMPOUND

Anal. Calcd. for $C_{13}H_9SO_4Ha2H_2O$		C: 46.20	H: 7.38
Found.		C: 46.90	H: 7.77

DETERMINATION OF ROTATORY POWER OF THE SEMICARBAZONE: Ethanol was added to 0.0359g. of the sample till the total

volume was 10 ml., at the temperature of 12°C. The value of -0.25 was obtained for the solution:

$$[\alpha]_D^{12} = \frac{100 \times (-0.26)}{1 \times 0.0359 \times 10} = -69.6$$

DETERMINATION OF ABSORPTION MAXIMA OF THE VARIOUS SEMICARBAZONE (CROTON ALDEHYDE, MESITYL OXIDE, α -PROPYLACROLEINE AND METHYL ETHYL KETON SEMICARBAZO-

NE):

Each sample was dissolved in ethanol in suitable concentration and the absorption maxima were determined by means of photoelectrotube. The results obtained were:

The sample from	max.
Houttuynia cordata	< 2500 Å
Methyl ethyl keton-semicarbazone	2500 Å
Mesithyl oxide-	2630 Å
Croton aldehyde-	2650 Å
α-Propyl acrolein-	2620 Å

DETERMINATION OF MOLECULAR WEIGHT OF THIOSEMICARBAZON: The molecular weight

was determined according to the Rast's method.

(1) Campher (176°C) 10.19mg.
Sample 0.991mg.

Depression in the melting point was:
176°C - 167°C = 19°C

Molecular weight: Found..... $\frac{+39.7 \times 1.70 \times 1000}{19 \times 10.19} = 230$

Calcd. for $C_{13}H_{18} = NNHCSNH_2$ = 260

(2) Campher (176°C) 13.22mg.
Sample 1.70mg.

Depression in the melting point was:
176°C - 153°C = 23°C

Molecular weight: Found..... $\frac{+39.7 \times 1.70 \times 1000}{23 \times 13.22} = 200$

Calcd. for $C_{13}H_{18} = NNH-C-SNH_2$ = 260

Summary

(1) An antifungal and optically active aldehyde which developed color towards Cu-acetate and ferri chloride has been isolated from Houttuynia cordata Thumb.

(2) The new aldehyde has been

assumed to be α-keto aldehyde of chemical composition: $C_{13}H_{18}O_2$, on the basis of results obtained by elementary analysis and determinations of molecular weight, absorption maximum and rotatory power.

Aknowledgements

The authors wish to express their gratitudes to Professor H. Tamiya and Professor E. Ochiai for their interest in this work and to the Ministry of Education for a grant in aid and to the Kowa Institute for Chemical Research for the aid to one of them.

They also thank Dr. G. Kobayashi, K. Shibata and members of the Takaoka Factory of Nippon Soda Co. Ltd. for assistant in the determination of rotatory power, absorption maxima and elementary analysis respectively.

(Received Feb. 25, 1951)