The Bitter Substance, Produced in Black-rotten Sweet Potato. II. On the Constitution of Ipomoeamarone. Part 1

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In a previous report,[1] some properties of ipomoeamarone, the main constituent of the bitter subtance obtained from black-rotten sweet potato, have been reported. Now I report more findings about its functional groups and degradation products.

Crude ipomoeamarone was isolated as the fraction, b.p. 140–155°/7 mm., from neutral part of the ethereal extract of sweet potato which was inoculated with *Ceratostomella fimbriata*. The semicarbazone, $C_{16}H_{25}O_3N_3$, m.p. 131–2°, and oxim, $C_{15}H_{23}O_3N$, b.p. 153–6°/6mm., were obtained from this fraction. Pure ipomoeamarone was regenerated from the semicarbazone by hydrolysis with oxalic acid, and it accorded with formula $C_{15}H_{22}O_3$; b.p. 146–9°/5 mm., d_4^{20} 1.0290, n_D^{20} 1.4808, $[\alpha]_D^{2^-}+10.0°$.

It is obvious by its attitude to potassium permanganate and bromine that ipomoeamarone is an unsaturated compound. By catalytic reductions, free ipomoeamarone absorbed 2 or 3 mols of hydrogen according to conditions, but the products could not lead to the crystalline derivatives. If the semicarbazone was hydrogenated, it gave tetrahydroipomoeamarone semicarbazone, $C_{16}H_{29}O_3N_3$, m.p. 95°, taking 2 mols of hydrogen. The hydrogenated compounds did not absorb bromine, but decolorised potassium permanganate after some minutes. Under some condition, the semicarbazone absorbed 3 mols of hydrogen, but the products did not crystallise, and hydrolysed ketone was tetrahydroipomoeamarone, $C_{15}H_{26}O_3$, b.p. 180° (bath)/5 mm. The ketone did not absorb bromine, but decolorised potassium permanganate after some minutes. The fact that dihydrocompound could not be obtained by stopping reduction when it absorbed one mol of hydrogen, shows two ethylenic linkages having same resistance to hydrogen.

With sodium and alcohol, ipomoeamarone formed an alcohol, ipomoeamarol, b.p. 162°/9 mm., which gave no ketonic reactions, and was derived to 3, 5-dinitrobenzoyl ester which, although liquid, gave the crystalline additional product with α-naphthylamine, m.p. 107–9°.

By catalytic reduction, ipomoeamarol absorbed 3 mols of hydrogen, but the product could not be made into crystalline derivatives. This fact leads to the conclusion that two ethylenic linkages cannot be in the $\alpha\beta$-position to the carbonyl group, nor conjugated with each other.

Of three oxygen atoms, one was confirmed to be ketone. The other two were probably oxide types, since all the reactions about hydroxyl groups, including Zerewitinoff-Fraschenträger method, were negative. In spite of the presence of three oxygen atoms, ipomoeamarone is liquid and it is difficult to obtain crystalline compounds from its derivatives; these facts, also, prove the absence of hydroxyl group in the molecule.

Although I cannot yet give evidences of whether two oxydic oxygens are aliphatic ether, cyclic ether, peroxide, or methylene-dioxide, it is rational to suppose that ipomoeamarone is a derivative of sesquiterpene and is an open-chain diolefinic ketone containg two oxide rings.

By oxidation of ipomoeamarone with potassium permanganate at room temperature, oxalic acid and a liquid keto-acid (supposed to be $C_{12}H_{20}O_4$) were obtained. For the latter, we propose the name ceratonic acid after the genus name of the fungus, *Ceratostomella fimbriata*.

This acid will be discussed in my next report.

By oxidation of ipomoeamarone semicarbazone at 100°, acetone, acetic acid, oxalic acid and a liquid acid were obtained. Production of acetone shows the presence of an isopropyl group in the molecule, and this suggests that it is a terpenic substance.

When a drop of ipomoeamarone or ipomoeamarol was added to a solution of vanillin in concentrated hydrochloric acid, pink color was produced and it turned gradually to dark red, then violet. Ipomoeamarone gave, also, color reactions by acetic anhydride and sulfuric acid (turning from blue-violet to brown), and glacial acetic acid and sulfuric acid (turning from dark red to brown). It is interesting that all of these color reactions are common through many terpenic compounds which contain oxide groups.

(1) T. Ohno and T. Takeuchi, *Botyu-Kagaku (Scientific Insect Control)* **12**, 26-9 (1949).

F. H. McDowall has been isolated ngaione[2] (pronounced "ny-one") which resembles to ipomoeamarone, from the essential oil of the leaves and terminal branchlets of *Myoporum laetum* of New Zealand. He has reported; ngaione, $C_{15}H_{22}O_3$, the main fraction of the essential oil, was a lemon-yellow oil with faint odour, b.p. 182–3°/27 mm., d_{20}^{20} 1.0276, $[\alpha]_D$ -26.20°, n_D^{20} 1.4804, the semicarbazone, m.p. 120–2° (decomp.), *p*-nitrophenylhydrazone, m.p. 103°, and was an open-chain compound with two non-conjugated double bonds, one ketonic group, and two separated oxide rings. Although his work has been interrupted and the results of his research have taken no definite form, many resemblances of the properties of both subtances and their derivatives suggest that these are mutually optical isomers, or, at least, analogous substances.

Recently, H. Watanabe and H. Iwata[3] reported nearly the same recognitions about ipomoeamarone.

Experimental

Ipomoeamarone.—Sweet potato (518 kg.) was treated as reported in a previous paper, and 125 kg. of dry black-rotten sweet potato was extracted with ether by a large scale Soxhlet extraction apparatus in batches of about 20 kg. About 6 kg. of extract was obtained. Its neutral part, obtained by treatment with aqueous alkali, was a reddish-brown, extremely bitter oil. The oil was fractionated.

B.p.	up to 141°/7 mm.	799 g.
	141–147°/7 mm.	686 g.
	147–160°/7 mm.	237 g.
	over 160°/7 mm.	93 g.
Total		1,815 g.

Residue *ca.* 1 kg.

Repeated distillation of these fractions gave the following fractions:

Lower fraction	b.p.	up to 140°/7 mm.	
Fraction 1.	b.p.	140–145°/7 mm.	467 g.
Fraction 2.	b.p.	145–150°/7 mm.	517 g.
Fraction 3.	b.p.	150–155°/7 mm.	262 g.
Higher fraction	b.p.	over 155°/7 mm.	

The physical constants and the analytical values of these main fractions were as follows:

Fraction 1,	d_4^{15} 1.0353,	n_D^{15} 1.4869,	$[\alpha]_D^{15}$ 13.3° (*c*, 17.5 in benzene)
Fraction 2,	1.0351,	1.4859,	15.2° (*c*, 18.4 in benzene)
Fraction 3,	1.0346,	1.4880,	13.5° (*c*. 19.2 in benzene)

Anal-Found: Fraction 1, C, 71.24; H, 7.17%. Fraction 2, C, 73.23: H, 8.30%. Fraction 3, C, 71.09; H, 9.04%. Calcurated for $C_{15}H_{22}O_3$: C, 72.00; H, 8.80%.

Ipomoeamarone Semicarbazone.—A mixture of 100 g. of crude bitter oil (above-mentioned fractions), 46 g. of semicarbazide hydrochloride, 40 cc. of pyridin, 200 cc. of alcohol and 100 cc. of water was allowed to stand at room temperature. After a few days the crystals of the semicarbazone were deposited. It was filtered, once dissolved in alcohol for the isolation of disemicarbazide, concentrated and recrystallised with dilute ethyl alcohol repeatedly. M.p. 131–2°, $[\alpha]_D^{29}$+85.0° (*c*, 2.0 in benene). The pyridine method gave better yield in shorter time than sodium acetate method.

Hydrolysis of the Semicarbazone.—A mixture of 6 g. of the semicarbazone and 6 g. of oxalic acid in 100 cc. of water was distilled with steam. From the distillate, pure ipomoeamarone was isolated with ether. B.p. 145–9°/5 mm., $[\alpha]_D^{27}$+10.0° (*c*. 2.5 in benzene), d_4^{20} 1.0290, n_D^{20} 1.4808, $[R]_D$ 69.0 (calc. for $C_{15}H_{22}O_3$, F_2; 69.43). (*Anal*. Found: C, 71.89; H, 9.02%. Calc. for $C_{15}H_{22}O_3$: C, 72.00; H, 8.80%.)

It gave the same semicarbazone again, but the yield was low; probably it was accompanied by a certain amount of racemisation.

Ipomoeamarone Oxim.—A mixture of 50 g. of the crude bitter oil (fraction 1), 14 g. of hydroxylamine hydrochloride, 11.5 g. of sodium carbonate, 40 cc. of water and 100 cc. of alcohol was refluxed on the water bath. After fifteen hours, alcohol was distilled off, ether was added, and this was followed by washing with dilute acid and alkali, and an ethereal layer was dried and concentrated. The residue was fractionated.

b.p.	118–133°/6 mm.	30 g.
b.p.	153–156°/6 mm.	11 g.

The first fraction, non-oximable oil was a pale yellow, mobile liquid, giving negative color reaction with sodium nitroprusside; d_4^{15} 1.0087, $[\alpha]_D^{15}$ +12.8° (*c*, 12.5 in benzene), n_D^{15} 1.4850. (Found: C, 75.44; H, 9.21)

The second fraction, ipomoeamarone oxim, was a pale yellow, very viscous liquid; d_4^{15} 1.0633, $[\alpha]_D^{15}$ +23.3° (*c*, 6.0 in benzene), n_D^{15} 1.5032. $[R]_D$ 73.7 (calc. for $C_{15}H_{23}O_3N$, F_2: 73.91). (*Anal*. Found: C, 67, 39; H, 8.38; N, 5.24%. Calc. for $C_{15}H_{23}O_3N$: C, 67.90; H, 8.68; N, 5.28%.)

Hydrogenation of the Crude Bitter Oil.—One gram of crude bitter oil in presence of 0.5 g. of Pd-$BaSO_4$ and 10 cc. of alcohol absorbed 225 cc. (2.5 mols) of hydrogen during nine hours. The resulting oil was a pale yellow oil of sweet odour

(2) F. H. McDowall, *J. Chem. Soc.*, **1925**, 220; **1927**, 731; **1928**, 1324.

(3) H. Watanabe and H. Iwata, Lecture at the meeting of Agricultural Chemical Society of Japan, 3rd Nov. 1951.

and decolorised $KMnO_4$ only after a few minutes. But it did not give any crystalline derivatives.

Hydrogenation of Ipomoeamarone Semicarbazone.—1) The semicarbazone (3.07 g.) in 55 cc. of ethyl acetate was treated with a stream of hydrogen and 2.00 g. of Pd-$BaSO_4$. During nine hours, 492 cc. (2.2 mols) of hydrogen were absorbed. The reduced product crystallised by treatment with dilute alcohol.

Tetrahydroipomoeamarone semicarbazone, m.p. 95–6°, was soluble in common organic solvents except petroleum ether, did not absorb bromine and decolorised $KMnO_4$ only slowly. (*Anal.* Found: C, 61.70; H, 9.25; N, 13.58%. Calc. for $C_{16}H_{29}O_3N_3$: C, 61.73; H, 9.33; N, 13.51%.)

The oil, obtained by treatment of the hydrogenated semicarbazone with dilute mineral acid or aqueous oxalic acid, gave color reaction with sodium nitroprusside.

Other experiments of hydrogenation derived to the same tetrahydroipomoeamarone semicarbazone as follows;

a) Semicarbazone 0.45 g., acetone 16 cc., Pd-$BaSO_4$ 0.45 g. Absorbed H_2 60 cc. (1.8 mols), during 2 hrs.
b) Semicarbazone 0.92 g., alcohol 15 cc., Pd-$BaSO_4$ 1.0 g. Absorbed H_2 186 cc. (2.8 mols), during 12 hrs.
c) Semicarbazone 0.92 g., alcohol 20 cc., PtO_2 0.05 g. Absorbed H_2 183 cc. (2.7 mols), during 6.5 hrs.

2) One gram of the semicarbazone in presence of 0.50 g. of Pd-$BaSO_4$ and 25 cc. of ethyl alcohol absorbed 232 cc. (3.12 mols) of hydrogen during thirteen hours. The product was a very viscous oil which did not crystallised for a long period. This was treated with aqueous oxalic acid. The resulting pale yellow oil (720 mg.), which gave color reaction with sodium nitroprusside, was distilled twice under 5 mm. (bath temp. 180°), yielding 410 mg. It did not absorb bromine, decolorised $KMnO_4$ after a few minutes, kept colorless for long time, and was shown to be tetrahydroipomoeamarone by analysis. (*Anal.* Found: C, 71.13, 70.82; H, 10.13, 10.39%. Calc. for $C_{15}H_{24}O_3$: C, 71.43; H, 9.52%. Calc. for $C_{15}H_{24}O_3$: C, 70.87; H, 10.24%. Calc. for $C_{15}H_{26}O_3$: C, 70.31; H, 10.94%)

Half-Hydrogenation of Ipomoeamarone Semicarbazone.—Five grams of the semicarbazone in 50 cc. of ether was shaken with 2.5 g. of Pd-$BaSO_4$ in the stream of hydrogen. Reaction was interrupted at the absorption of one molecule of hydrogen. Repeated crystallisation of the resulting product yielded ipomoeamarone semicarbazone (m.p. 128°, and there was no depression of melting point with the specimens which melt at 131°). After the decolorisation of total half-hydrogenated products with active carbon, reduction was continued and tetrahydroipomoeamarone semicarbazone was obtained after the absorption of another molecule of hydrogen.

Reduction of Ipomoeamarone with Sodium and Alcohol; Ipomoeamarol.—Five grams of crude ipomoeamarone was reduced with 5 g. of sodium and 100 cc. of alcohol. The product, which boiled at 162°/9 mm. (3.33 g.), was a pale yellow oil, having a bitter taste, hardly ever colorised with sodium nitroprusside, and decolorised $KMnO_4$ at once.

A 0.3 g. portion of the substance in 10 cc of benzene was refluxed with 0.5 g. of 3, 5-dinitrobenzoyl chloride and a few drops of pyridine on the water bath for half an hour. 3, 5-Dinitrobenzoyl ester (0.44 g.), thus obtained, was a very viscous oil and did not crystallise.

To 0.4 g. of the liquid ester, a solution of 0.2 g. of α-naphthylamine in 80% alcohol was added. Addition products of α-naphthylamine were separated, m.p. 107–9°, dark-red crystals, but could not be purified because of their unstability.

Ipomoeamarol (0.85 g.) in alcohol was hydrogenated with 0.50 g. of Pd-$BaSO_4$. About 3 mols (228 cc.) of hydrogen was absorbed during ten hours. The pale yellow oil obtained, did not produce any crystalline derivatives.

Analysis of the Active Hydrogen by Zerewitinoff-Fraschenträger Method.—By the analysis, ipomoeamarone, regenerated from the semicarbazone, showed absence of active hydrogen.

111.6 mg. of substance; 0.02 cc. of CH_4 (15°, 759 mm.). Calcurated for one active hydrogen; 10.00 cc.

Oxidation of Ipomoeamarone with Potassium Permanganate at Room Temperature.—A 1.8 g. portion of ipomoeamarone, which was regenerated from the semicarbazone, was suspended in 50 cc. of water. Small portions of powdered $KMnO_4$ were added to the mixture successively under shaking and occassional cooling with water. Four and a quarter grams (8.55 atoms of oxygen) of $KMnO_4$ were required. Manganese dioxide was removed by filtration and washed with hot water. There were no neutral substances in the oxidised solution. Then, after this solution was concentrated, it was acidified with dilute sulfuric acid, and was distilled with steam. The distillate required only a small amount of aqueous alkali by titration. The non-volatile part was, then, extracted with ether. The extract (1.06 g.) was a brown viscous oil, and gave ketonic reaction with sodium nitroprusside. By distillation under 4.5 mm. (bath temp. 145–190°), 0.45 g. of the oil was obtained, which gave neither semicarbazone, nor 2, 4-dinitrophenylhydrazone, showed negative iodoform reaction, and was with difficulty soluble in cold water. Three months later, the crystals grew in the oil. After five months, large crystals were picked up and washed with ether. This was proved to be oxalic acid (m.p. 98°) by mixed melting point determination and analysis. (*Anal.* Found: C, 20.17; 19.95; H, 5.21, 5.12%. Calc. for $C_2H_2O_4 \cdot 2H_2O$: C, 19.05; H, 4.76%.)

The liquid acid, separated from oxalic acid, was redistilled under 5 mm. (167–180° bath temp.). It gave ketonic reaction with sodium nitroprusside. For this liquid keto-acid, I suggest the name ceratonic acid. This will be discussed in my next report.

Oxidation of Ipomoeamarone Semicarbazone with Potassium Permanganate at 100°.—Five grams of the semicarbazone was suspended in 100 cc. of boiling water. Small portions of powdered $KMnO_4$ were added successively. During the operation, vapor from the top of the reflux condenser was lead to the solution of 2, 4-dinitrophenylhydrazine (mixture of 0.5 g. of 2, 4-dinitrophenylhydrazine, 2.0 cc. of H_2SO_4, and 20 cc. of alcohol). About 43 g. (25 atoms of oxygen) of $KMnO_4$ were required. From the solution of 2, 4-dinitrophenylhydrazine orange-yellow crystals were isolated. This, after several recrystallisations from alcohol, was proved to be acetone 2, 4-dinitrophenylhydrazone (m.p. 127°) through mixed melting point determination and analysis. (*Anal.* Found: C, 45.76, 45.70; H, 4.08, 4.39; N, 23.57, 23.75%. Calc. for $C_9H_{10}O_4N_4$: C, 45.38; H, 4.20; N, 23.53%.)

From the oxidised solution, no other neutral product was isolated except a small amount of the recovered semicarbazone (m.p. 129°). As to volatile acid, acetic acid was caught as the *p*-bromophenacyl ester (m.p. 82°) and proved by mixed melting point determination and analysis. (*Anal.* Found: C, 46.73, 46.41; H, 3.68, 3.41%. Calc. for $C_{10}H_9O_3Br$: C, 46.69; H, 3.50%.) As to non-volatile acid, crystalline and liquid acids were obtained by ether extraction. The former was proved to be oxalic acid through mixed melting point determination and analysis. (*Anal.* Found: C, 19.59, 19.47; H, 4.87, 5.39%. Calc. for $C_2H_2O_4 \cdot 2H_2O$: C, 19.05; H, 4.76%.) The latter was distilled under 6 mm. (bath temp. 170–200°). The pale yellow oil gave negative reaction with sodium nitroprusside.

Summary

Ipomoeamarone is an open-chain ketone with two oxide rings and two ethylenic linkages. It gives a liquid keto-acid and oxalic acid by oxidation with potassium permanganate at room temperature, and acetone, acetic acid, oxalic acid and a liquid acid by oxidation with the same reagent at 100°.

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