

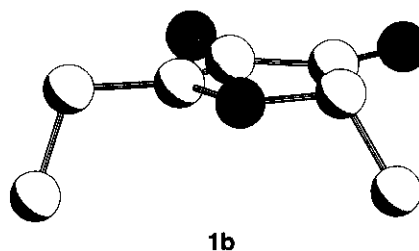
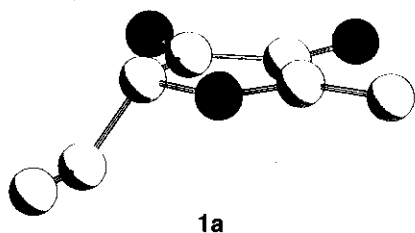
Homofuronol: A Powerful Tool to Prepare and Improve Sophisticated High Quality Flavors

By Ulrich A. Huber

Givaudan-Roure Research Ltd., Dübendorf, Switzerland

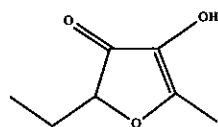
Homofuronol [**1a** and **1b**] is a quite recently introduced flavor chemical which has only been marketed since 1988.¹ It belongs to a class of structurally related flavoring compounds like furonol [**2**], maltol [**3**], corylone [**4**] and others.

They all contain cyclic 3-alkyl-2-enol-1-one structures [**5**] in a planary arrangement, and they develop related agreeable flavor impressions of sweet, caramel, roasted types.



Homofuronol

2-Ethyl-4-hydroxy-5-methyl-3(2H)-furanone +
5-Ethyl-4-hydroxy-2-methyl-3(2H)-furanone



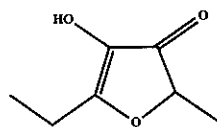
3 parts

Mwt 142.1 C₇H₁₀O₃

CAS 27538-10-9 (major tautomer) and
27538-09-6

Legislation: Nature identical

Occurrence: Coffee, shoyu (=fermented soy hydrolysate),
melon



1 part

FEMA 3623

Organoleptic Properties: Sweet, caramel, fruity, bread-like
Uses: Fruit flavors (fresh and dried) exotic fantasy, caramel,
coffee, maple, meat, bread, tobacco

Dosage: 0.1-50 ppm

Additional Names: Homofuraneol³
Sugarone⁴

Physical Data of Pure Material: bp 82-83°C/0.2 Torr (with
some decomposition)

Appearance: Clear slightly yellowish liquid

Solubility: Miscible with water, ethanol, organic esters and
diols, poorly soluble in pentane, etc.

Specific Gravity: d₂₀²⁰: 1.137

Refractive Index: n_D²⁰: 1.511

Flash Point: 65°C

Physical Data of 20% Solution in Propylene Glycol

Appearance: Clear yellowish liquid

Specific Gravity: d₂₀²⁰: 1.048-1.058

Refractive Index n_D²⁰: 1.440-1.450

Flash Point TCC: 65°C/149°F

Some of these cycloenol-ones also enhance and modify flavors. They are weakly acidic due to their phenolic-like structure and are soluble in water (see Table I).

Other representatives of this class of flavor compounds are maltol [**3a**]⁵ (R=CH₃); ethyl maltol [**3b**]⁵ (R=C₂H₅); 2-hydroxy-3-methylcyclopent-2-enone (corylone)[**4**]⁶ and a number of its alkylated homologues;⁷ and 2-hydroxy-3-methyl-4-ethylbutenolide [**6**] (R=C₂H₅)⁸ and its methyl homologue [**6**] (R=CH₃).^{9,10} Homologues of homofuronol [**1**] are the often used furonol (also "furanol") [**2**]¹¹ on one side, and the commercially not available norfuronol on the other [**7**].^{12,13}

Homofuronol was isolated from shoyu¹³ (fermented soy hydrolysate), coffee¹⁴ and just recently from melon.¹⁵ It was found to be the strongest representative of the group of three furanones [**1**, **2** and **7**] mentioned above, according to its flavor threshold. It is said to be 3 to 9 times stronger than furonol in the range of its application dose probably because of its higher lipophilicity which raises its vapor pressure and its odor value.¹⁶ It exists in two tautomeric forms [**1a**] and [**1b**] in a ratio of ~3:1 having a sweet, caramel, fruity and bread-like flavor.

History

Homofuronol was first mentioned in 1967/1969 in two patents^{17,18} which were followed by two publications^{3,19} in the chemical literature.

In 1976 homofuronol was isolated from shoyu (fermented soy hydrolysate) by a Japanese group.²⁰ In a following paper they gave some more details and they claimed that homofuronol is the main and most important constituent of the characteristic "good flavor" of shoyu.¹³ Increasing homofuronol concentrations are improving the quality of shoyu. As shoyu is used as a flavor enhancer and Chinese people consider their food as "naked" without the presence of soy sauce,²¹ it may imply that homofuronol itself possesses a flavor-enhancing and modifying effect in addition to its own flavor contribution.

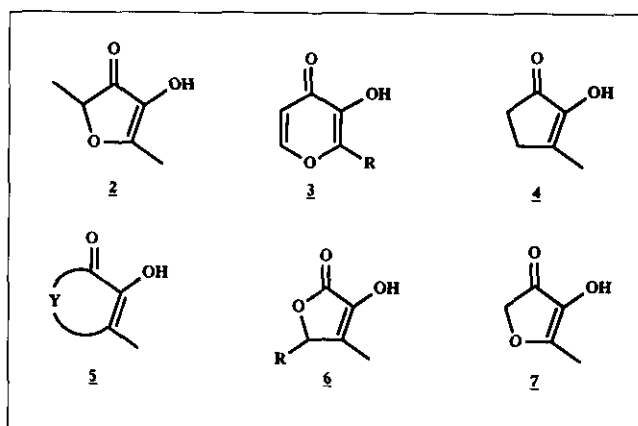
In 1978 a second natural occurrence of homofuronol was found when it was isolated from coffee.¹⁴ In 1991 it was identified in muskmelon¹⁵—this time in fresh and untreated food material. The homofuronol content in shoyu is claimed to be 50 to 100 ppm¹³ whereas in coffee it is 2 to 8 ppm.¹⁴ This means that Japanese people have a per capita consumption of 750 mg homofuronol per year based on an average annual per capita consumption of 10 l shoyu. In Germany, on the other hand, the per capita intake would be 33 mg homofuronol per year on the basis of an average annual per capita consumption of 6.6 kg coffee.

Application

Organoleptically, homofuronol belongs to the same family as maltol and furonol (furanol), two classical chemicals in the flavor industry, but it is stronger. When used on its own or in combination with maltol and furonol, one can observe interesting and very pleasant olfactive results, and in quite a few cases price advantages are also achieved.

Table I. Flavor thresholds in water (in ppb) of structurally related compounds

1	21	4	61,000
2	158	6 (R = C ₂ H ₅)	0.024
3a (R = CH ₃)	2800	7	8,300
3b (R = C ₂ H ₅)	44		



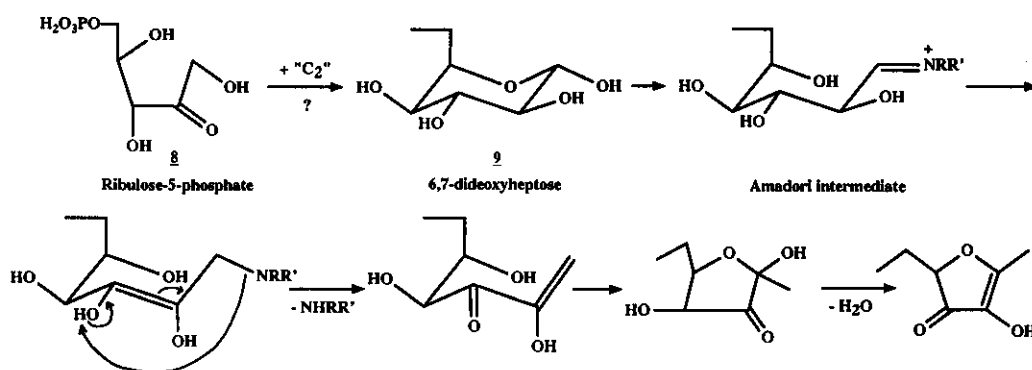
However, it cannot generally be recommended to completely substitute maltol or furonol with homofuronol in existing flavors, even though they are of the same flavor profile, as one will definitely experience a difference in the end product. You will find that homofuronol has less caramel, cooked or roasted notes. It is extremely useful in flavor creation, on its own or in combination, as it will give natural, sweet, round, juicy fruit notes. It also increases the body and mouthfeel which is very noticeable in the final application. Its versatility permits its use in almost all types of flavors, as well as for fragrance material.²²

Analytical Methods and Toxicology

As homofuronol is a polar molecule which it cannot be extracted from aqueous preparations by hydrocarbons but rather by methylene chloride, or in a separation procedure as a weak acidic fraction.¹³ In the ferric chloride test a purple-colored reaction can be observed. UV, IR, NMR and mass spectra have been published.²⁰ As for chromatographical methods, HPLC is the method of choice (e.g. on a C₁₈ reversed phase column in acetonitrile/water = 2:8, or analogous to H. Lee²³). Both tautomers [**1a** and **1b**] can be detected by UV (maximum absorbance at 290 nm). But gas chromatography can also be used where one or both tautomers are detected, depending on the conditions used (e.g. fused silica capillary column).²⁴ Tressl used silylated material for semiquantitative homofuronol detection by GC/MS.¹⁴ Another method of testing the purity of homofuronol is NMR with an internal standard such as hexamethyldisiloxane or vanillin.

A 90-day feeding study in rats yielded no adverse effects at a dose level of 1.43 mg/kg.²⁵ An LD-50 p.o. was determined as 2800 mg/kg/d in the mouse. Assuming an average

Homofuronol



daily intake of 0.04 mg/kg/d, this corresponds to a "safety factor" of 70,000.

Biosynthesis

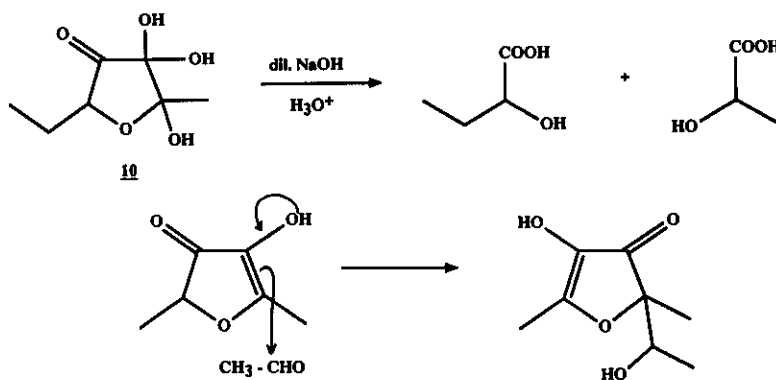
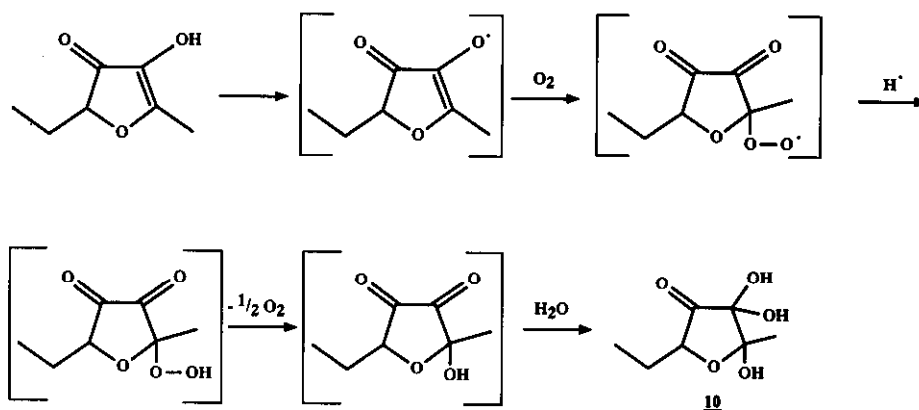
Sasaki proposes a biosynthetic access to homofuronol by treating sugars with yeasts under conditions related to the fermentation procedure of shoyu.²⁶ He was able to prove that the metabolic pentose cycle is an early stage in this synthesis, where intermediates like ribulose-5-phosphate [8] are important precursors.

But the further steps of this synthesis remain unknown. The required chain elongation by two carbon atoms would be similar to the known sedoheptulose-7-phosphate formation, but would occur at a lower oxidation state. In analogy to the mechanistic hypothesis of Hodge²⁷ for the formation of furonol [2] ("pseudo-reduction" $C_6H_8O_3$) from an Amadori intermediate of rhamnose or for the formation of norfuronol [7]²⁸ from an Amadori product of a pentose, a 6,7-dideoxyheptose [9] would be a reasonable intermediate for the final homofuronol formation (Scheme 1).

A biomimetic synthesis involves condensing a C_4 and a C_3 unit with aldolase. It was developed by Wong et al.²⁹

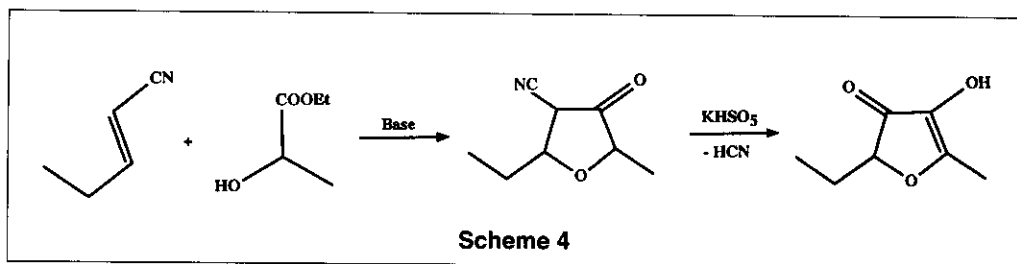
Purity and Stability

Homofuronol is usually sold as pure material (99% by GC) or as a 20% solution in propylene glycol. Its purifica-



tion is not without problems because by distillation or chromatography its decomposition might be more dominant than the purification effect.

When stored in the absence of light and air (e.g. under nitrogen) in a dry and cold (4°C) location, it is perfectly



stable for months. Freshly prepared material might taste milder and less burnt than stored material. Old samples often get a smell of acetic acid.

The stability of homofuronol in water may be compared to the respective data of furonol³⁰ where half of the material was decomposed after 12 days at room temperature at pH 7, or after 100 days at room temperature or 6 hours at 100°C, respectively, at pH 4, where it shows its highest stability.

Tautomeric Equilibrium

Homofuronol normally exists in two tautomeric forms [**1a**, **1b**], in a ratio of 3:1 to 2:1, which are in a slow equilibrium with each other. If the pure tautomeric mixture is stored for years in a freezer, it crystallizes where the main

tautomeric form [**1a**] is favored and accumulates. It is possible to isolate the main tautomeric form [**1a**] by crystallization from water; m.p. 36-37, 5°C. The crystals are relatively stable, but as soon as they melt or dissolve, they tautomerize to the equilibrium mixture. The two tautomeric forms can easily be seen analytically by HPLC or by NMR.

Reactivity and Decomposition

Like furonol, homofuronol is sensitive to oxygen. It forms an oxygenated product [**10**] among other decomposition products. A mixture of diastereomers of [**10**] was identified upon decomposition of homofuronol. The ¹³C/¹H-correlated 2-D NMR spectra were measured and found to be consistent with the empirical formula described by Nunomura.¹³ Scheme 2 illustrates one proposed method for the formation of [**10**].

This product [**10**] can easily be prepared by stirring a solution of homofuronol in diisopropyl ether in the presence of air for a few days and by isolating the precipitate. This product is soluble in water and easily falls apart in base, yielding lactic- and α-hydroxy-butyric acid (Scheme 3).

Not unexpectedly, homofuronol is sensitive to electrophilic attack at the enolic center. Such reactions are used to describe, for example, the reaction of furonol [**2**] with aldehydes.³¹

Upon heat treatment of homofuronol, the first products which can be observed analytically and sensorially are acetic- and propionic acids.

Synthesis

Quite a few chemical accesses of homofuronol are described in the literature and in various patents. Most of them are just modifications of a furonol synthesis.^{3,19,29,32-38} However, only a few are of commercial value.

One very short route (Scheme 4) which is commercially applied by Givaudan is the condensation of pentene nitrile and ethyl lactate followed by oxidation using aqueous monoperoxisulfate.^{36,38}

Acknowledgments: *The author would like to thank G. Frater, H. Küntzel, R. Teyssier and H. J. Wild for their discussions, help and interest in this review.*

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Address correspondence to Ulrich A. Huber, Givaudan-Roure Research Ltd., Ueberlandstrasse 138, CH-8600 Dübendorf, Switzerland

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