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(54) **Title:**
OXALAMIDE DERIVATIVE AS UMAMI FLAVOURING AGENT

(57) **Abstract:**
The compound of the formula (1) is novel and is useful in conferring umami taste on consumable compositions, such as foodstuffs and beverages.

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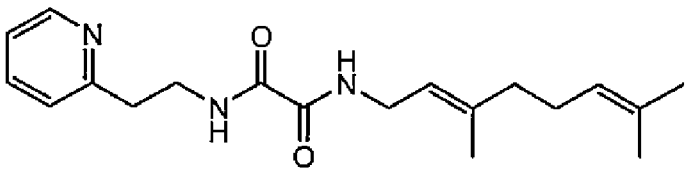
(54) Title: OXALAMIDE DERIVATIVE AS UMAMI FLAVOURING AGENT



(1)

(57) Abstract: The compound of the formula (1) is novel and is useful in conferring umami taste on consumable compositions, such as foodstuffs and beverages.

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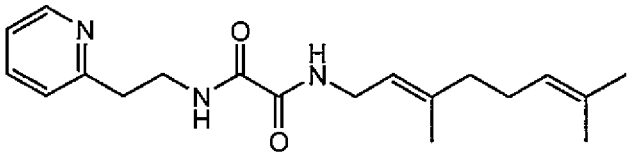
OXALAMIDE DERIVATIVE AS UMAMI FLAVOURING AGENT

This disclosure relates to a novel molecule and its use in creating umami flavour.

Umami is a flavour sensation generally associated with Asian cuisine. In addition, improved umami taste helps make low salt products more palatable. Umami flavour has traditionally been achieved by the addition of monosodium glutamate (MSG) to foodstuffs. However, the presence of MSG in foodstuffs is not universally welcome, and there is an interest in the achievement of umami taste with lower proportions of MSG than is normally the case.

It has now been found that it is possible to achieve umami taste with a reduced proportion of MSG, or even the complete elimination of umami. This is achieved by means of a novel compound. There is therefore provided a compound of the formula (1)



(1)

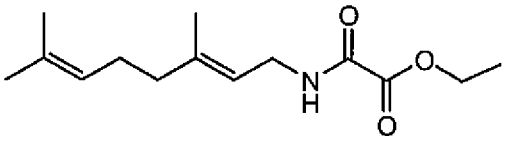
There is further provided a umami flavour composition, comprising flavour ingredients and a umami-enhancing or –providing proportion of a compound of the formula (1).

There is further provided a consumable composition having umami flavour, said umami flavour being at least partially provided by the presence therein of a compound of the formula (1).

There is further provided a method of conferring umami flavour on a consumable composition, comprising the addition to the composition of a compound of the formula (1).

The compound of formula (1) (hereinafter referred to as "the Umami Compound") exists in two isomeric forms, the *E*-form and the *Z*-form. Both of these compounds are comprehended by the formula (1), and both may be used, either in pure form or in a mixture of isomers. The *E*-form is N1-neryl-N2-(2-(pyridin-2-yl)ethyl)oxalamide and the *Z*-form N1-geranyl-N2-(2-(pyridin-2-yl)ethyl)oxalamide.

The Umami Compound may be prepared by methods well known to the art. One such method involves the preparation of (*E*)-ethyl-2-(3,7-dimethylocta-2,6-dienylamino-2-oxoacetate

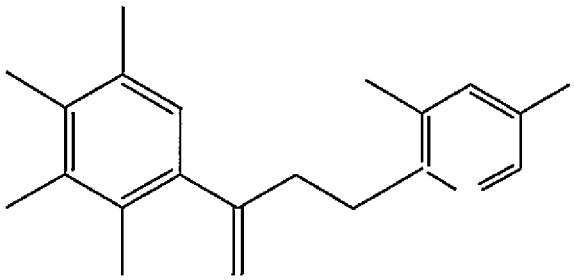


by reaction of geranylamine with diethyl oxalate. This product is then reacted with 2-(pyridin-2-yl)ethanamine. Precise details are set forth in the examples.

It has been surprisingly found that the Umami Compound not only confers a high degree of umami flavour and at very low dosages, but also that this flavour is of unusual quality, in that it has a clean, non-artificial taste. This is in contrast to many other non-MSG umami flavourants.

The Umami Compound may be used alone, or it may be mixed with other flavouring ingredients to provide a flavouring composition ready for addition to a consumable composition. The flavouring ingredients may include other umami flavourants, including MSG. Use of the Umami Compound allows a considerable reduction in MSG levels, and in some cases the complete elimination of MSG.

Particular examples of other umami compounds that are useful in this application are compounds (including salts thereof) according to Formula (2)



(2)

in which

R^1 is selected from H, methyl and ethyl;

R^2 is selected from H, OH, fluorine, C_1-C_4 linear or branched alkyl, C_1-C_6 alkoxy wherein the alkyl group is linear or branched, or comprises or consists of a C_3-C_5 cycloalkyl moiety;
R^3 is selected from H and methoxy;
or R^2 and R^3 together form a bridging moiety $-O-CH_2-O-$ between the phenyl carbon atoms to which they are connected;
R^4 is selected from OH and methoxy; and
R^5 and R^6 are independently selected from H and methyl;
R^1, R^2, R^3, R^4, R^5 and R^6 being selected such that,
(i) when R^2 and R^3 together form a bridging moiety $-O-CH_2-O-$ between the phenyl carbon atoms to which they are connected, R^1, R^5, R^6 are H, and R^4 is OH; and
(ii) when R^4 is OH and R^1-R^3 are H, at least one of R^5, R^6 is methyl.

In a particular embodiment, R^2 is selected from H, OH, fluorine, methyl, C_1-C_6 alkoxy wherein the alkyl group is linear or branched, or comprises or consists of a C_3-C_5 cycloalkyl moiety.

In a further particular embodiment, R^2 is selected from methyl, methoxy and isobutyloxy, R^3 is H, R^4 is OH and R^5 and R^6 are H.

Such compounds are described in UK patent application No. 0913804. Particular non-limiting examples of such compounds include:
1-(2-hydroxy-4,5-dimethylphenyl)-3-(pyridine-2-yl)propan-1-one;
1-(2-hydroxy-4-methylphenyl)-3-(pyridin-2-yl)propan-1-one;
1-(2-hydroxy-4-methoxyphenyl)-3-(pyridin-2-yl)propan-1-one;
1-(2-hydroxy-4-isobutoxyphenyl)-3-(pyridine-2-yl)propan-1-one.

Other non-limiting examples of suitable compounds include:

N1-(2-methoxy-4-methylbenzyl)-N2-(2-pyridin-2-yl-ethyl) oxalamide;
N1-(2,4-dimethoxybenzyl)-N2-(2-pyridin-2-yl-ethyl) oxalamide;
N1-(2-methoxy-3-methylbenzyl)-N2-(2-(-5methyl)pyridin-2-yl-ethyl) oxalamide;
N-heptan-4-yl benzo(D)-1,3-dioxole 5-caboxamide;
N(3,7-dimethyl-2,6-octadien-1-yl) cyclopropyl carboxamide ;

cyclopropane carboxylic acid 2-isopropyl-5-methyl-cyclohexyl amide.

Other non-limiting examples of umami flavour-conferring and -enhancing compounds that may be used with the Umami Compound include those described in EP 1642886, WO 2005/015158, EP 1312268, WO 2003/088768, EP 1291342 and WO 2006/003107.

The proportion of the Umami Compound used will depend on the nature of the use and the effect desired. For example, the proportion needed for a partial replacement of MSG will naturally be lower than that of a complete MSG replacement. The proportion may vary between wide limits, typically between 0.1 ppm and 10 ppm by weight of a consumable composition, more particularly between 0.5 ppm and 5 ppm. However, these are general indications only of useful proportions, and the skilled flavourist may use proportions outside these ranges for particular effects.

By "consumable composition" is meant any composition that is taken into the mouth for ultimate spitting out or ingestion. The composition may be in any physical form, solid, liquid or gaseous. Non-limiting examples include all food products, food additives, nutraceuticals, pharmaceuticals and any product placed in the mouth including (but not limited to) chewing gum, oral care products, and oral hygiene products including but not limited to, cereal products, rice products, tapioca products, sago products, baker's products, biscuit products, pastry products, bread products, confectionery products, dessert products, gums, chewing gums, flavor or flavor-coated food/beverage containers, yeast products, baking-powder, salt and spice products, snack foods, savoury products, mustard products, vinegar products, sauces (condiments), soups, seasonings, ready-to-eat meals, gravies, nuts & nut products, , processed foods, vegetable products, meat and meat products, egg products, milk and dairy products, yoghurts, cheese products, butter and butter substitute products, milk substitute products, soy products, edible oils and fat products, , beverages, carbonated beverages, alcoholic drinks such as beers, wines and spirits, non-alcoholic drinks such as soft drinks, including forms requiring reconstitution including, without limitation, beverage powder, milk based beverage powder, sugar-free beverage powder, beverage syrup, beverage concentrate, coffee and tea, food extracts, plant extracts, meat extracts, condiments, gelatins, pharmaceutical and non-pharmaceutical gums, tablets,

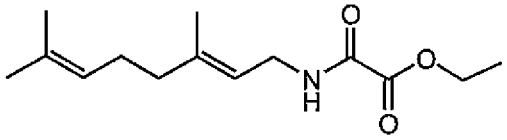
lozenges, drops, emulsions, elixirs, syrups and other preparations for making beverages, and combinations thereof.

The disclosure is further described with reference to the following non-limiting examples, which depict particular embodiments.

Example 1

Preparation procedure for N1-geranyl-N2-(2-(pyridin-2-yl)ethyl)oxalamide

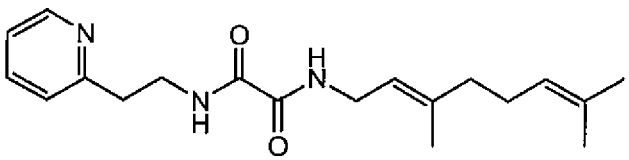
Step 1: preparation of (*E*)-ethyl-2-(3,7-dimethylocta-2,6-dienylamino-2-oxoacetate



Geranylamine (5 g, 32.6 mmol) was added dropwise to diethyl oxalate (15 g, 103 mmol) to give a colorless solution. The solution was heated to 120C and stirred at this temperature for 2 hours; the formed ethanol was distilled off during the reaction. The excess of diethyl oxalate was removed by vacuum distillation until 160°C/ 1mbar. 8.1g (93% yield) of brownish residual oil was obtained. The product is ca. 95% pure according to NMR analysis

^{1}H-NMR in $CDCl_3$ (ppm): 1.26-1.41(3H, t, COOCH2-C**H3**), 1.60(3H, s, CH2-C(C**H3**)=CH-), 1.68(6H, s, (C**H3**)$_2$-C=CH-), 2.01(2H, m, -CH2-C**H2**-C(CH3)=CH -), 2.08(2H, m, (CH3)$_2$-C=CH-C**H2**-CH2), 3.89(2H, t, CH2-C(CH3)=CH-C**H2**-NH-), 4.22-4.38(2H, q, COOC**H2**-CH3) 5.07(1H, m, (CH3)$_2$-C=C**H**-CH2-), 5.20(1H, m, CH2-C(CH3)=C**H**-CH2-NH-), 7.37(1H, s, CON**H**-CH2-CH=C(CH3)-CH2)

Step 2: preparation of N1-geranyl-N2-(2-(pyridin-2-yl)ethyl)oxalamide



The ethyl 2-(3,7-dimethylocta-2,6-dienylamino)-2-oxoacetate (1.5 g, 5.92 mmol) was mixed with 2-(pyridin-2-yl)ethanamine (1 g, 8.19 mmol) in ethanol (20 ml) to give a yellow

solution. The reaction mixture was stirred at reflux for 1.5hour. Then the solvent was removed by evaporation. The remaining residual solid was washed with ethanol/ pentane to provide the target compound as white crystals (1.3g; 65% yield). The product is ca. 97% pure according to NMR analysis.

^{1}H-NMR in $CDCl_3$ (ppm): 1.60(3H, s, CH2-C(C**H3**)=CH-), 1.68(6H, s, (C**H3**)$_2$-C=CH-), 2.01(2H, m, -CH2-C**H2**-C(CH3)=CH -), 2.08(2H, m, (CH3)$_2$-C=CH-C**H2**-CH2), 3.04(2H, t, NH-CH2-C**H2**-pyridinyl), 3.89(2H, t, CH2-C(CH3)=CH-C**H2**-NH-), 3.76(2H, q, NH-C**H2**-CH2-pyridinyl), 5.07(1H, m, (CH3)$_2$-C=C**H**-CH2-), 5.20(1H, m, CH2-C(CH3)=C**H**-CH2-NH-), 7.14-7.16(2H, m, 2x C**H** from pyridinyl), 7.37(1H, s, CON**H**-CH2-CH=C(CH3)-CH2), 7.61(1H, t, C**H** from pyridinyl), 8.15(1H, s, CON**H**-CH2-CH2-pyridinyl), 8.57(1H, m, C**H** from pyridinyl)

Example 2

Testing of compound.

Two solutions were prepared:

A - a solution of 0.3% NaCl and 0.05 % MSG

B - a solution of 0.3% NaCl and 3 ppm of N1-geranyl-N2-(2-(pyridin-2-yl)ethyl)oxalamide.

The samples were tasted by a professional panel composed of 2 women and 3 men aged between 30 and 60. The panel agreed that both solutions tasted umami. They also agreed that solution B was slightly stronger umami, had more succulence and sweetness and had more lingering savoury notes.

Example 3

Testing of compound

Two solutions were prepared:

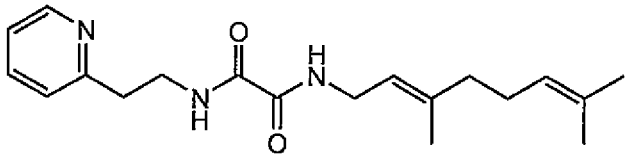
A - a solution of 0.5% NaCl , 0.15 % MSG and 0.025 % Ribonucleotide mixture

B - a solution of 0.5% NaCl, 0.05 % MSG, 0.010% Ribonucleotide mixture and 1.5 ppm of N1-geranyl-N2-(2-(pyridin-2-yl)ethyl)oxalamide.

The samples were tasted by a professional panel composed of 2 women and 3 men aged between 30 and 60. The panel agreed that both solutions were of equal umami strength.

Claims:

1. A compound of the formula (1)



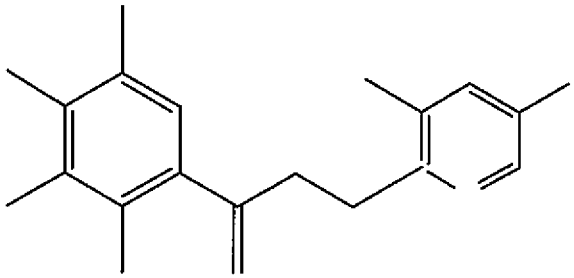
(1)

2. The compound N1-neryl-N2-(2-(pyridin-2-yl)ethyl)oxalamide.

3. The compound N1-geranyl-N2-(2-(pyridin-2-yl)ethyl)oxalamide.

4. A umami flavour composition, comprising flavour ingredients and a umami-enhancing or –providing proportion of a compound according to any one of claims 1-3.

5. A umami flavour composition according to claim 4, in which the composition additionally comprises at least one compound (including salts thereof) according to the Formula (2)



(2)

in which

R^1 is selected from H, methyl and ethyl;

R^2 is selected from H, OH, fluorine, C_1-C_4 linear or branched alkyl, C_1-C_6 alkoxy wherein the alkyl group is linear or branched, or comprises or consists of a C_3-C_5 cycloalkyl moiety;

R^3 is selected from H and methoxy;

or R^2 and R^3 together form a bridging moiety $-O-CH_2-O-$ between the phenyl carbon atoms to which they are connected;

R^4 is selected from OH and methoxy; and

R^5 and R^6 are independently selected from H and methyl;

R^1, R^2, R^3, R^4, R^5 and R^6 being selected such that,

(i) when R^2 and R^3 together form a bridging moiety $-O-CH_2-O-$ between the phenyl carbon atoms to which they are connected, R^1, R^5, R^6 are H, and R^4 is OH; and

(ii) when R^4 is OH and R^1-R^3 are H, at least one of R^5, R^6 is methyl.

6. A consumable composition having umami flavour, said umami flavour being at least partially provided by the presence therein of a compound according to any one of claims 1-3.

7. A consumable composition according to claim 6, in which a compound according to any one of claims 1-3 is present to the extent of from 0.1 ppm and 10 ppm, more particularly between 0.5 ppm and 5 ppm, by weight of a consumable composition.

8. A method of conferring umami flavour on a consumable composition, comprising the addition to the composition of a compound according to any one of claims 1-3.

9. A method according to claim 8, in which a compound according to any one of claims 1-3 is present to the extent of from 0.1 ppm and 10 ppm, more particularly between 0.5 ppm and 5 ppm, by weight of a consumable composition.