(51) International Patent Classification:
C11B 9/00 (2006.01) C07C 323/12 (2006.01)


(21) International Application Number:
PCT/IB2006/051419

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(22) International Filing Date: 5 May 2006 (05.05.2006)

(25) Filing Language: English

(30) Priority Data:
PCT/IB2005/001449 13 May 2005 (13.05.2005) IB

(71) Applicant (for all designated States except US): FIRMENICH SA [CH/CH]; 1, route des Jeunes, P.O. Box 239, CH-1211 Geneva 8 (CH).

(72) Inventors; and

(75) Inventors/Applicants (for US only): ESCHER, Sila Dorothée [CH/CH]; 12, Rampe De Chavant, CH-1232 Conflignon (CH). NICLASS, Yvan [CH/CH]; 27C, Route De Certoux, CH-1258 Perly (CH). SAUDAN, Lionel [CH/CH]; 36, Rue Prévost-martin, CH-1205 Geneva (CH).

(74) Agent: SALVATERRA-GARCIA, Maria de Lurdes; Firmenich SA, P.O. Box 239, CH-1211 Geneva 8 (CH).

Published:
— with international search report
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: THIOLS AS FLAVORING INGREDIENT

(57) Abstract: The present invention concerns the use of a 3-mercaptopheptyl carboxylate, in the form of any one of its stereoisomers or mixture thereof, as flavoring ingredient, in particular to impart fruity, teas and citrus aftertaste. Said compounds provide long-lastingness to the flavors composition in which they are added.
THIOLS AS FLAVORING INGREDIENT

Technical field

The present invention relates to the field of flavor. More particularly, it concerns the use of a 3-mercaptoheptyl carboxylate, in the form of any one of its stereoisomers or mixture thereof, as flavoring ingredient, in particular to impart fruity, teas and citrus aftertaste with a well-balanced long-lastingness. The present invention concerns also the compositions or articles containing said compound.

Prior art

To the best of our knowledge, amongst the invention's compounds, only 3 mercaptoheptyl acetate has been reported in the literature (see S.Collin et al. in J.Agr.Food Chem, 2003, 3618) and only in the form of a crude reaction mixture. This acetate is described as having odor notes of the "onion, exotic fruit, candy" type. However, this prior art document does not report or suggest any flavor properties of the compounds of formula (I), or any use of said compound in the field of flavor.

Description of the invention

As mentioned above, the invention concerns the use as flavoring ingredient of 3-mercaptoheptyl carboxylate, of formula

![Chemical Structure](image)

(I)

in an optically active or non-optically active form, wherein $R^1$ represents a C1-C3 alkyl group.

According to a particular embodiment of the invention, the acetate derivatives, $R^1$ representing a methyl group, are particularly appreciated for their flavors.

The invention's compounds are valuable flavoring ingredients capable of imparting fruity, citrus and/or teas bottom notes, which results in a very good and appreciated aftertaste or long-lastingness of the flavor.
In general a flavor is characterized by its top notes as well as the bottom notes, the former defining the first impression in the mouth and the latter determining the impression in the month and the length of the organoleptic effect. Flavoring ingredients capable of imparting well-balanced bottom notes are relatively rare and for that reasons highly desirable for the flavorists.

In particular, by means of non-limiting examples of the invention, one may cite 3-mercaptoheptyl acetate which possesses a relatively weak top note reminding of a peach, citrus and tea tonality. This top note is followed by highly appreciated and performing bottom notes of the green/black tea type as well as of the citrus-grapefruit and fruity-peach type which render said compound a very useful flavoring ingredient.

The two enantiomers of the cited acetate, namely the (R) and the (S) ones, are also valuable flavoring ingredients, which can be used in a similar way. Amongst said enantiomers the most appreciated is the (S) one, which has a taste very close to the one of the racemate, although its grapefruit type note is weaker than the one of the racemate.

The invention’s compounds are derivatives of 1-methoxy-3-heptanethiol, described in EP 1249446, and are structurally close to 3-mercaptohexyl acetate or butanoate, described by K.-H. Engel in J.Agr.Food Chem, 1991, 2249.

However, despite the structural resemblance between compounds (I) and those of the prior art, the former have flavor properties quite unexpected and distinct. 1-Methoxy-3-heptanethiol is described as having tropical fruit and, in particular, berries flavor notes, while 3-mercaptohexyl acetate is described as having an extremely fruity flavor, suggestive of passion fruit with a Riesling type note.

In particular, 3-mercaptoheptyl acetate distinguishes itself from the cited prior art compounds by having an original flavor profile and especially aftertaste. As will be shown hereinbelow by the examples, 3-mercaptoheptyl acetate distinguishes itself from 1-methoxy-3-heptanethiol by not having a tropical fruit character as well as by its much weaker top notes and its much more pronounced aftertaste, as well as by the presence of teas and pear-peach notes which are absent from the prior art compound.

Furthermore, 3-mercaptoheptyl acetate distinguishes itself from 3-mercaptohexyl acetate by its overall flavor profile and in particular by not having the typical sulfury, guava-passion fruit note of the prior art compound.
Another object of the present invention is a compound of formula (I), as defined above, in an optically active form. Indeed said enantiomer-enriched form is new as the prior art cited above mentions only a racemate.

As mentioned above, the invention concerns the use as perfuming ingredients of the compounds of formula (I). In other words, it concerns a method to confer, enhance, improve or modify the flavor properties, and in particular its long-lastingness, of a flavoring composition or of a flavored article, which method comprises adding to said composition or article an effective amount of at least a compound of formula (I).

By “use of a compound of formula (I)” it has to be understood here also the use of any composition containing compound (I) and which can be advantageously employed in the flavors industry as active ingredients.

Said compositions, which in fact can be advantageously employed as flavoring ingredient, are also an object of the present invention.

Therefore, another object of the present invention is a flavoring composition comprising:
i) as flavoring ingredient, at least one invention’s compound as defined above;
ii) at least one ingredient selected from the group consisting of a flavor carrier and a flavor base; and

iii) optionally at least one flavor adjuvant.

By “flavor carrier” we mean here a material which is practically neutral from a flavor point of view, i.e., that does not significantly alter the organoleptic properties of flavoring ingredients. Said carrier may be a liquid or a solid.

As liquid carrier one may cite, as non-limiting examples, an emulsifying system, i.e., a solvent and a surfactant system, or a solvent commonly used in flavors. A detailed description of the nature and type of solvents commonly used in flavor cannot be exhaustive. However, one can cite as non-limiting example solvents such as dipropylene glycol, diethyl phthalate, isopropyl myristate, benzyl benzoate, 2-(2-ethoxyethoxy)-1-ethanol or ethyl citrate, which are the most commonly used. As non-limiting examples of solvents commonly used in flavors, one can cite compounds such as propylene glycol, triacetine, triethyl citrate, benzylic alcohol, ethanol, vegetal oils or terpenes.
As solid carrier one may cite, as non-limiting examples, absorbing gums or polymers, or yet encapsulating materials. Examples of such materials, for example, may comprise wall-forming and plasticizing materials, such as mono-, di- or trisaccharides, natural or modified starches, hydrocolloids, cellulose derivatives, polyvinyl acetates, polyvinylalcohols, proteins or pectins, or yet the materials cited in reference texts such as H. Scherz, Hydrokolloids: Stabilisatoren, Dickungs- und Gehermittel in Lebensmittel, Band 2 der Schriftenreihe Lebensmittelchemie, Lebensmittelqualität, Behr's VerlagGmbH & Co., Hamburg, 1996. The encapsulation is a well known process to a person skilled in the art, and may be performed, for instance, using techniques such as spray-drying, agglomeration or yet extrusion; or consists of a coating encapsulation, including coacervation and complex coacervation techniques.

Generally speaking, by “flavor base” we mean here a composition comprising at least one flavoring co-ingredient.

Said flavoring co-ingredient is not of the formula (I). Moreover, by “flavoring co-ingredient” it is meant here a compound, which is used in flavoring preparation or composition to impart a hedonic effect. In other words such a co-ingredient, to be considered as being a flavoring one, must be recognized by a person skilled in the art as being able to impart or modify in a positive or pleasant way the taste of a composition, and not just as having a taste.

The nature and type of the flavoring co-ingredients present in the base do not warrant a more detailed description here, which in any case would not be exhaustive, the skilled person being able to select them on the basis of its general knowledge and according to intended use or application and the desired organoleptic effect. In general terms, these flavoring co-ingredients belong to chemical classes as varied as alcohols, aldehydes, ketones, esters, ethers, acetates, nitriles, terpene hydrocarbons, nitrogenous or sulphurous heterocyclic compounds and essential oils, and said flavoring co-ingredients can be of natural or synthetic origin. Many of these co-ingredients are in any case listed in reference texts such as the book by S. Arctander, Perfume and Flavor Chemicals, 1969, Montclair, New Jersey, USA, or its more recent versions, or in other works of a similar nature, as well as in the abundant patent literature in the field of flavor. It is also
understood that said co-ingredients may also be compounds known to release in a controlled manner various types of flavoring compounds.

According to a particular embodiment of the invention’s, particularly appreciated flavor bases are those capable of imparting top notes of the citrus-grapefruit, teas and/or peach type and/or red fruit (e.g. berries or tropical). Indeed, with such flavor bases, the compounds of formula (I) are capable of providing a highly appreciated long-lastingness of the flavor.

Generally speaking, by “flavor adjuvant” we mean here an ingredient capable of imparting additional added benefit such as a color, a particular light resistance, chemical stability, etc. A detailed description of the nature and type of adjuvant commonly used in flavoring bases cannot be exhaustive, but it has to be mentioned that said ingredients are well known to a person skilled in the art.

An invention’s composition consisting of at least one compound of formula (I) and at least one flavor carrier represents a particular embodiment of the invention as well as a flavoring composition comprising at least one compound of formula (I), at least one flavor carrier, at least one flavor base, and optionally at least one flavor adjuvant.

It is useful to mention here that the possibility to have, in the compositions mentioned above, more than one compound of formula (I) is important as it enables the flavorist to prepare accords, flavors, possessing the flavor tonality of various compounds of the invention, creating thus new tools for their work.

Preferably, any mixture resulting directly from a chemical synthesis, e.g. without an adequate purification, in which the compound of the invention would be involved as a starting, intermediate or end-product could not be considered as a flavoring composition according to the invention.

Moreover, a compound of formula (I) can be advantageously incorporated into flavored articles to positively impart, or modify, the taste of said articles. Consequently, a flavored article comprising:

i) as flavoring ingredient, at least one compound of formula (I), as defined above, or an invention’s flavoring composition; and

ii) a foodstuff base,

is also an object of the present invention.
For the sake of clarity, it has to be mentioned that, by “foodstuff base”, we mean here an edible product, e.g. a food or a beverage. Therefore, a flavored article according to the invention comprises the functional formulation, as well as optionally additional benefit agents, corresponding to a desired edible product, e.g. a foods or beverages, and a flavor effective amount of at least an invention’s compound.

The nature and type of the constituents of the foodstuffs or beverages do not warrant a more detailed description here, which in any case would not be exhaustive, the skilled person being able to select them on the basis of its general knowledge and according to the nature of said product.

Non-limiting examples of suitable foodstuff bases include a bakery, a dairy, a confectionary, a savory, an infusion, a soft drink, a flavored water and a juice product. In particular one may cite foodstuff bases such as a chewing gum, a yogurt, milk, a hot or cold tea drink, a carbonated or non-carbonated soft drinks, potato chips, a soup, a fruit juice.

The proportions in which the compounds according to the invention can be incorporated into the various aforementioned articles or compositions vary within a wide range of values. These values are dependent on the nature of the article to be flavored and on the desired organoleptic effect as well as the nature of the co-ingredients in a given base when the compounds according to the invention are mixed with flavoring co-ingredients, solvents or additives commonly used in the art.

In the case of flavoring compositions, typical concentrations are in the order of 0.5 % to 5% by weight, or even more, of the compounds of the invention based on the weight of the consumer product into which they are incorporated. Concentrations lower than these, such as in the order of 0.01% to 0.5% by weight, can be used when these compounds are incorporated into flavored articles, percentage being relative to the weight of the article.

The invention will now be described in further detail by way of the following examples, wherein the abbreviations have the usual meaning in the art, the temperatures are indicated in degrees centigrade (°C) ; the NMR spectral data were recorded in CDCl₃ (if not stated otherwise) with a 400 MHz machine for ¹H and ¹³C, the chemical
displacements \( \delta \) are indicated in ppm with respect to TMS as standard, the coupling constants \( J \) are expressed in Hz.

**Example 1**

5

**Synthesis of 3-mercaptopheptyl acetate**

**A) 3-Hydroxyheptyl acetate**: To an ice-cooled and stirred solution of heptane-1,3-diol (6.60 g, 50 mmol) in pyridine (50 ml) was added dropwise acetic acid chloride (3.92 g, 50 mmol). The stirring was continued at room temperature for 16. Workup with diethyl ether and flash chromatography (cyclohexane-ethyl acetate 75:25) gave 6.00 g of the desired acetate (69%).

\(^1\)H-NMR (after exchange with D\(_2\)O): 4.33 \((ddd, J = 11.3, 8.7, 8.2, 1 \text{ H})\); 4.16 \((dt, J = 11.3, 5.6, 1 \text{ H})\); 3.66 \((m, 1 \text{ H})\); 2.06 \((s, 3 \text{ H})\); 1.82, 1.67, 1.43, 1.32 \((4 \text{ m, 8 H})\); 0.91 \((t, J = 7.1, 3 \text{ H})\).

\(^{13}\)C-NMR: 171.49 \((s)\); 68.68 \((d)\); 61.88 \((t)\); 37.24 \((t)\); 36.32 \((t)\); 27.81 \((t)\); 22.71 \((t)\); 21.01 \((q)\); 14.06 \((q)\).

**B) 3-(Acetyltio)heptyl acetate**: To a solution of 1,3-dimethyl-2-fluoropyridinium 4-methylbenzenesulfonate (4.90 g, 16.5 mmol) in acetone-benzene 1:1 \((v/v, 40 \text{ ml})\), triethylamine (2.3 ml, 16.5 mmol) was added, followed by the acetate obtained under A) (2.61 g, 15 mmol). The clear solution was stirred for 1 h. Thioacetic acid (1.17 ml, 16.5 mmol) and triethylamine (2.3 ml, 16.5 mmol) in acetone-benzene 1:1 \((5 \text{ ml})\) were added. The mixture was heated at 80\(^\circ\text{C}\) (bath temperature) for 3 hour. The solvents were then partly removed at *in vacuo*. Workup (diethyl ether) followed by purification of the crude product \((3.73 \text{ g})\) by flash chromatography with cyclohexane-ethyl acetate 9:1 afforded 1.44 g (41\%) of desired product in 94\% purity.

\(^1\)H-NMR: 4.13 \((t, J = 6.5, 2 \text{ H})\); 3.61 \((m, 1 \text{ H})\); 2.32 \((s, 3 \text{ H})\); 2.06 \((s, 3 \text{ H})\); 1.99, 1.84, 1.61, 1.33 \((4 \text{ m, 8 H})\); 0.89 \((t, J = 7.2, 3 \text{ H})\).

\(^{13}\)C-NMR: 195.49 \((s)\); 171.07 \((s)\); 61.98 \((t)\); 41.24 \((d)\); 34.65 \((t)\); 33.64 \((t)\); 30.76 \((q)\); 28.88 \((t)\); 22.47 \((t)\); 20.97 \((q)\); 13.96 \((q)\).
C) 3-Mercaptoheptanol: To an ice-cooled and stirred suspension of LiAlH₄ (285 mg, 7.5 mmol) in diethyl ether (40 ml) was added dropwise a solution of thioacetate obtained under B) (1.16 g, 5 mmol) in diethyl ether (30 ml). Workup with diethyl ether gave 770 mg of crude mercaptoalcohol that was purified by flash chromatography (pentane-diethyl ether 7:3) and the desired compound was obtained as colorless oil (680 mg, 92%).

¹H-NMR (after exchange with D₂O): 3.83 (m, 2 H); 2.94 (m, 1 H); 1.98, 1.67 1.51 1.33 (4 m, 8 H); 1.41 (d, J = 7.7, 1 H), 0.91 (t, J = 7.6, 3 H).

¹³C-NMR: 60.76 (t); 41.32 (t); 39.29 (t); 38.03 (d); 29.18 (t); 22.42 (t); 14.02 (q).

D) 3-Mercaptoheptyl acetate: To a stirred solution of the alcohol obtained under C) (444 mg, 3 mmol) in dichloromethane (2 ml) was added dropwise a solution of acetic acid chloride (236 mg, 3 mmol) in dichloromethane (1 ml). After 3 hours, the reaction mixture was concentrated to ca. 1 ml in a Vigreux apparatus, and the concentrate was purified by flash chromatography with pentane-diethyl ether 95:5 as eluant. The desired compound was obtained as colorless oil (400 mg, 70%).

¹H-NMR: 4.24 (m, 2 H); 2.87 (m, 1 H); 2.05 (s, 3 H); 2.02, 1.73, 1.69, 1.49, 1.33 (5 m, 8 H); 1.40 (d, J = 7.6, 1 H), 0.92 (t, J = 7.1, 3 H).

¹³C-NMR: 171.00 (q), 62.27 (t); 38.83 (t); 37.75 (t); 37.62 (d); 29.13 (t); 22.41 (t); 20.97 (q); 14.00 (q).

Example 2

Synthesis of the enantiomers of 3-mercaptoheptyl acetate

(R)-1,3-Heptanediol was obtained according to the procedure described in EP 1249446.

(S)-Methyl 3-hydroxyheptanoate was obtained according to W. Oppolzed et al. in Tetrahedron Letters, 1992, pg 2439.

A) Preparation of (S)-3-Mercaptoheptyl Acetate

i) (R)-3-hydroxyheptyl acetate

To a solution at 0°C of (R)-1,3-heptanediol (9.703g, 73 mmol) in pyridine (74 ml) was added dropwise over a period of 45 minutes neat acetyl chloride (5.3 ml, 74 mmol). The reaction is slightly exothermic and a heavy white precipitate formed
immediately. At the end of the addition, the white slurry was further stirred at room temperature for 100 minutes. Then the reaction mixture was poured into a mixture of ice and H$_2$SO$_4$ 2N and extracted several times with Et$_2$O. The organic layers were combined, washed successively with H$_2$SO$_4$ 2N, H$_2$O, aqueous saturated NaHCO$_3$, brine and dried over anhydrous Na$_2$SO$_4$. After filtration, the solvent was removed under vacuum to give the crude compound. Purification by flash chromatography on silica gel eluted with a mixture of heptane/AcOEt (8/2) to give the desired product (9.404 g, 68%) as a pale yellow liquid.

Optical rotation: $\alpha_D = -7.0 \circ$ (c = 5.0, CHCl$_3$, 20°C).

$^1$H-NMR: 4.33 (ddd, $J = 11.3$, 5.6, 5.1, 1H), 4.15 (dt, $J = 11.3$, 5.6, 1H), 3.67 (br m, 1H), 2.17 (br d, $J = 0.6$, 1H), 2.06 (s, 3H), 1.87-1.77 (m, 1H), 1.72-1.62 (m, 1H), 1.52-1.24 (m, 6H), 0.91 (t, $J = 7.3$, 3H).

$^{13}$C-NMR: 171.5 (s), 68.7 (d), 61.9 (t), 37.2 (t), 36.3 (t), 27.8 (t), 22.7 (t), 21.0 (q), 14.1 (q).

ii) (R)-3-[(Methylsulfonyl)oxy]heptyl acetate

To a solution at 0°C of (R)-3-hydroxyheptyl acetate (9.211 g, 49 mmol) in Et$_2$O (170 ml) was added Et$_2$N (20 ml, 142 mmol, 3 eq), followed by methanesulfonyl chloride (5.7 ml, 73 mmol, 1.5 eq). The cooling bath was removed and the reaction mixture was stirred at room temperature. After 90 minutes, the reaction mixture was poured into ice/water mixture and extracted several times with Et$_2$O. The organic layers were combined and washed with aqueous HCl 0.5 M, H$_2$O and dried over anhydrous Na$_2$SO$_4$. After filtration, the solvent was removed under vacuum to give crude (R)-3-[(methylsulfonyl)oxy]heptyl acetate (12.615 g, 49 mmol) as a yellow oil which was directly taken into the next step.

$^1$H-NMR: 4.83 (quint, $J = 6.1$, 1H), 4.19 (t, $J = 6.4$, 2H), 3.02 (s, 3H), 2.06 (s, 3H), 2.05-1.98 (m, 2H), 1.8-1.7 (m, 2H), 1.45-1.3 (m, 4H), 0.92 (t, $J = 6.9$, 3H).

$^{13}$C-NMR : 170.9 (s), 80.2 (d), 60.2 (t), 38.6 (q), 34.5 (t), 33.4 (t), 26.9 (t), 22.4 (t), 20.9 (q), 13.9 (q).

iii) (S)-3-(Acetylthio)heptyl acetate
A 100 ml, four necked flask equipped with a mechanical stirring bar, a thermometer probe and an argon inlet/outlet was charged with cesium carbonate (9.58 g, 27 mmol, 1.1 eq) and NMP (45 ml). To this stirred pink suspension was added dropwise over 5 minutes thioacetic acid (4.9 ml, 69 mmol, 1.4 eq). The reaction mixture was further stirred at room temperature for 100 minutes. To this solution was added neat (R)-3-[(methylsulfonyl)oxy]heptyl acetate (12.615 g, 49 mmol). The reaction mixture was further stirred at room temperature for 20 hours and then poured into water and extracted several times with a heptane/toluene mixture (4/1). The organic layers were combined, washed with water and dried over anhydrous Na₂SO₄. After filtration and evaporation of the solvent under vacuum the crude product was purified by flash chromatography on silica gel eluted with a heptane/AcOEt (9/1) mixture to give pure (+)-(S)-3-(acetylthio)heptyl acetate (5.333 g, 47% over the two steps).

Optical rotation: α₀ = + 8.7 (c = 5.0, CHCl₃, 20°C).

¹H-NMR: 4.13 (t, J = 6.7, 2H), 3.65-3.58 (m, 1H), 2.32 (s, 3H), 2.05 (s, 3H), 2.03-1.94 (m, 1H), 1.89-1.79 (m, 1H), 1.7-1.5 (m, 2H), 1.45-1.25 (m, 4H), 0.89 (t, J = 6.9, 3H).

¹³C-NMR: 195.4 (s), 171.0 (s), 61.9 (t), 41.2 (d), 34.6 (t), 33.7 (t), 30.8 (q), 28.9 (t), 22.5 (t), 20.9 (q), 13.9 (q).

iv) (S)-3-Mercapto-1-heptanol

A 500 ml, four necked flask equipped with a mechanical stirring bar, a thermometer probe and an argon inlet/outlet was charged with LiAlH₄ (2.15 g, 56.7 mmol) and Et₂O (180 ml). The mixture was cooled at c.a. 0°C with an ice/water bath and a solution of (+)-(S)-3-(acetylthio)heptyl acetate (5.049 g, 22 mmol) in Et₂O (50 ml) was added over a period of 1 hour. More Et₂O (50 ml) was added to rinse. The cooling bath was removed and the reaction mixture was stirred at room temperature for 4 hours. Then, the reaction mixture was poured into ice, acidified with aqueous HCl 5N (100 ml), and extracted several times with Et₂O. The organic layers were combined and washed with water, aqueous saturated NaHCO₃, brine, and dried over anhydrous Na₂SO₄. After filtration and removal of the solvent under vacuum, the crude product was purified by flash chromatography on silica gel eluted with
pentane/Et₂O (95/5) and then with Et₂O to give pure (S)-3-mercaptop-1-heptanol (2.547 g, 79%).

Optical rotation: $\alpha_D = +4.4$ (c = 5.0, CHCl₃, 20°C).

$^1$H-NMR: 3.87-3.75 (m, 2H), 2.99-2.89 (m, 1H), 2.4 (brs, 1H), 2.01-1.92 (m, 1H), 1.72-1.6 (m, 2H), 1.57-1.44 (m, 2H), 1.43-1.25 (m, 2H), 1.41 (d, $J = 7.2$, 1H), 0.91 (t, $J = 7.2$, 3H).

$^{13}$C-NMR: 60.6 (t), 41.3 (t), 39.2 (t), 37.9 (d), 29.2 (t), 22.4 (t), 14.0 (q).

v) (S)-3-Mercaptoheptyl acetate

To a solution of (S)-3-mercaptop-1-heptanol (2.364 g, 16 mmol) in CH₂Cl₂ (10 ml) was added dropwise at room temperature a solution of acetyl chloride (1.2 ml, 13.9 mmol) in CH₂Cl₂ (6 ml) over a period of 20 minutes. After 4 hours of stirring at room temperature, the reaction mixture was poured into brine and extracted several times with Et₂O. The organic phases were combined, washed with brine and dried over anhydrous Na₂SO₄. After filtration and removal of the solvent under vacuum, the crude product was purified by flash chromatography on silica gel eluted with pentane/Et₂O (95/5), followed by Kugelrohr distillation under vacuum to give pure (S)-(3-mercaptopheptyl acetate (S-10) (2.195 g, 11 mmol, 72%) as an orange liquid.

Optical rotation: $\alpha_D = +7.3$ (c = 5.0, CHCl₃, 20°C).

$^1$H-NMR: 4.29-4.19 (m, 2H), 2.91-2.81 (m, 1H), 2.05 (s, 3H), 2.07-1.98 (m, 1H), 1.88-1.62 (m, 2H), 1.56-1.45 (m, 2H), 1.42-1.28 (m, 3H), 1.39 (d, $J = 7.2$, 1H), 0.91 (t, $J = 7.4$, 3H).

$^{13}$C-NMR: 170.95 (s), 62.3 (t), 38.8 (t), 37.76 (t), 37.6 (d), 29.1 (t), 22.4 (t), 20.9 (q), 14.0 (q).

B) Preparation of (R)-3-Mercaptoheptyl Acetate

i) (S)-1,3-Heptanediol

To a suspension of LiAlH₄ (7.52g, 198.2 mmol) in THF (100 ml) at 0°C was added slowly a solution of (S)-methyl 3-hydroxyheptanoate (15.06 g, 94 mmol) in THF (25 ml) over a period of one hour. At the end of the addition, more THF (10 ml) was added to rinse and the reaction mixture was stirred at room temperature for 5 hours.
and 30 minutes. More LiAlH₄ (3.76 g, 99 mmol) was then added, and the reaction mixture was stirred for another 17 hours. Next, the reaction mixture was cooled with an ice-water bath and the reaction was stopped by adding successively H₂O (11.5 ml), aqueous NaOH 30% (11.5 ml) and H₂O (34 ml). The resulting white slurry was dried by adding anhydrous Na₂SO₄ (46 g) and filtered over a plug of celite thoroughly washed with THF. The solvent was removed under vacuum and the crude diol was purified by flash chromatography on silica gel eluted with a mixture of heptane/AcOEt (2/1) to give the desired compound (9.910 g, 80%) as a pale yellow oil.

¹H-NMR: 3.9-3.75 (m, 3H), 3.38 (br s, 1H), 3.23 (br s, 1H), 1.76-1.59 (m, 2H), 1.56-1.23 (m, 6H), 0.91 (t, J = 7, 3H).

¹³C-NMR: 72.0 (d), 61.5 (t), 38.3 (t), 37.5 (t), 27.8 (t), 22.7 (t), 14.1 (q).

(R)-3-Mercaptoheptyl acetate was then obtained by following the same experimental procedure as described above under A). The spectroscopic properties of the enantiomer (R) were the same as for the enantiomer (S) at the exception of the optical rotation:

\[ \alpha_D = -7.5 \text{ (c = 5.0, CHCl}_3, 20^\circ\text{C)} . \]

**Example 3**

**Flavoring composition and flavored articles comprising 3-mercaptoheptyl acetate**

A flavor composition having a "grapefruit character" was prepared by admixing the following ingredients:

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Parts by weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nootkatone</td>
<td>0.1</td>
</tr>
<tr>
<td>Linalool</td>
<td>2.0</td>
</tr>
<tr>
<td>Ethyl butyrate</td>
<td>0.5</td>
</tr>
<tr>
<td>Terpineol</td>
<td>3.0</td>
</tr>
<tr>
<td>Acetaldehyde</td>
<td>1.0</td>
</tr>
<tr>
<td>Octanal</td>
<td>0.3</td>
</tr>
</tbody>
</table>
Decanal 0.1
Citronellal 2.0
Geranyl Acetate 0.5
1%* Bucchu oil 0.5

5 Ethanol 990.0
1000.0

* in ethanol

The addition of 1 part by weight of 3-Mercaptoheptyl acetate to the above described flavor composition provided a fruity-citrusy top note and imparted a long-lastingness of the citrus notes, giving a strong impression of juiciness, with slight bitterness reminding a tea aftertaste. The new composition thus obtained was named A).

When, instead of the invention’s compound there was added the same amount of 1-methoxy-3-heptanethiol, the composition acquired an enhanced sulfury top-note and no effect on the aftertaste and the juiciness was perceivable. The new composition thus obtained was named B).

When, instead of the invention’s compound there was added the same amount of 3-mercaptohexyl acetate the overall taste was changed in the direction of an overripe guava tonality, and no long-lastingness of the flavor was perceivable. The new composition thus obtained was named C).

When the compositions A), B), or C) were added into a carbonated soft drink at the level of 0.1% w/w in the finished drink. The organoleptic effects were similar to the ones described above. However, composition A) was also able to confer to the flavor of the finished drink a much impressive “body”/”fullness” comparable to that of grapefruit juice.

Example 4

Flavoring composition and flavored articles comprising 3-mercaptoheptyl acetate

A flavor composition having a “peach character” was prepared by admixing the following ingredients:
<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Parts by weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Octyl Acetate</td>
<td>5.00</td>
</tr>
<tr>
<td>Linalool</td>
<td>1.50</td>
</tr>
<tr>
<td>Gamma undecalactone</td>
<td>0.50</td>
</tr>
<tr>
<td>Delta decalactone</td>
<td>1.00</td>
</tr>
<tr>
<td>Isobutyric acid</td>
<td>3.00</td>
</tr>
<tr>
<td>Isopropyl methyl thiazol</td>
<td>0.05</td>
</tr>
<tr>
<td>1%* Ofmanthus essential oil</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Ethanol</strong></td>
<td><strong>987.95</strong></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1000.00</strong></td>
</tr>
</tbody>
</table>

* in ethanol

The addition of 1 parts by weight of 3-mercaptoheptyl acetate to the above-described flavor composition provided a peach skin top note and imparted a long-lastingness related to the peach character as well as a juicy-fleshy character. The new composition thus obtained was named A).

When, instead of the invention’s compound there was added the same amount of 1-methoxy-3-heptanethiol, the composition flavor profile became unbalanced and lacked of a long-lasting effect. The new composition thus obtained was named B).

When, instead of the invention’s compound there was added the same amount of 3-mercaptohexyl acetate the overall taste became clearly of the type overripe guava and loosed the peach taste. The new composition thus obtained was named C).

When the compositions A), B), or C) were added into a tea drink at the level of 0.05% w/w in the finished drink. The organoleptic effects were similar to the ones described above. However, composition A) was also able to enhance the tea character of the finished drink.
Claims

1. Use as flavoring ingredient of a compound of formula

   \[
   \begin{align*}
   &\text{SH} \\
   &\text{O} \\
   &\text{O} \\
   &\text{R}^1
   \end{align*}
   \]  

   (I)

   in an optically active or non-optically active form, wherein \( R^1 \) represents a \( C_1-C_3 \) alkyl group.

2. Use according to claim 1, characterized in that \( R^1 \) represents a methyl group.

3. A flavoring composition comprising:
   i) as flavoring ingredient, at least one compound of formula (I), as defined in claim 1 or 2;
   ii) at least one ingredient selected from the group consisting of a flavor carrier and a flavor base; and
   iii) optionally at least one flavor adjuvant.

4. A flavoring composition according to claim 3, characterized in that the flavor base has top notes of the citrus-grapefruit, teas and/or peach type and/or red fruit.

5. A flavored article comprising:
   i) as flavoring ingredient, at least one compound of formula (I), as defined in claim 1 or 2; and
   ii) a foodstuff base,

6. A flavored article according to claim 5, characterized in that foodstuff base is a bakery, a dairy, a confectionary, a savory, an infusion, a soft drink, a flavored water and a juice product.
7. A compound of formula

\[ \text{\begin{align*}
\text{R}^1 & \quad \text{SH} \\
\text{O} & \quad \text{O}
\end{align*}} \]

in an optically active or non-optically active form, wherein \( R^1 \) represents a C₁-C₃ alkyl group, provided that 3-mercaptohexyl acetate is excluded.

8. As a compound according to claim 7, (R)-3-mercaptohexyl acetate, (S)-3-mercaptohexyl acetate or an optically active mixture thereof.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

INV. C11B9/00 C07C323/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C11B C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td>GB 1 336 037 A (GIVAUDAN CIE SA L) 7 November 1973 (1973-11-07) claim 4</td>
<td>1-8</td>
</tr>
<tr>
<td>X</td>
<td>COLLIN S.; VERMEULEN, C.: &quot;Combinatorial Synthesis and Sensorial Properties of 21 \nMercapto Esters&quot; J. AGRIC. FOOD. CHEM., no. 51, 5 February 2003 (2003-02-05), pages \n3618-3622, XP002398286 cited in the application Compound 18; Table 2</td>
<td>1-8</td>
</tr>
</tbody>
</table>

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents:

*A* document defining the general state of the art which is not considered to be of particular relevance

*E* earlier document but published on or after the international filing date

*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

*O* document referring to an oral disclosure, use, exhibition or other means

*P* document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"A" document member of the same patent family

Date of the actual completion of the international search

11 September 2006

Date of mailing of the international search report

25/09/2006

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk
Tel. (+31-70) 940-2040, Tx. 31 651 epos nl, Fax: (+31-70) 940-3016

Authorized officer

Saunders, Thomas

Form PCT/ISA/210 (second sheet) (April 2005)
<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>EP 1 249 446 A (FIRMENICH SA) 16 October 2002 (2002-10-16) cited in the application example 4</td>
<td>1-8</td>
</tr>
<tr>
<td>Patent document cited in search report</td>
<td>Publication date</td>
<td>Patent family member(s)</td>
</tr>
<tr>
<td>---------------------------------------</td>
<td>-----------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CH 545775 A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DE 2155672 A1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>FR 2117625 A5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IT 1049522 B</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NL 7115451 A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>US 2003040460 A1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>US 2004037787 A1</td>
</tr>
</tbody>
</table>