

FLAVOR COMPOUNDS

The present invention relates to new 3-mercapto-alkanols, namely 3-mercapto-2-methyl-butan-1-ol and 3-mercapto-3-methyl-hexan-1-ol including their stereoisomers, to flavoring compositions and to food or beverage products flavored with at least one of these compounds and to a method for the preparation of both diastereoisomers of 3-mercapto-2-methyl-butan-1-ol.

In the food and beverage industry flavors play a critical role in the appreciation of food and beverage products. Hereafter the term flavor shall comprise as well flavor, as also aroma and/or taste and in the following context all these terms are used interchangeably.

Several mercapto-alkan-1-ol compounds have been identified as flavorant in food products. Thus, 3-mercapto-hexan-1-ol has been identified in the yellow passion fruit (*Passiflora edulis* f. *flavicarpa*) (K. -H. Engel, R. Tressel, *J. Agric. Food Chem.* 1991, 39, 2249), in Sauvignon blanc wine (T. Tominaga, A. Furrer, R. Henry, D. Dubourdieu, *Flavour Fragrance J.* 1998, 13, 159; P. Werkhoff, M. Güntert, G. Krammer, H. Sommer, J. Kaulen, *J. Agric. Food Chem.* 1998, 46, 1076) and in red Bordeaux wine (P. Bouchilloux, P. Darriet, R. Henry, V. Lavigne-Cruège, D. Dubourdieu, *J. Agric. Food Chem.* 1998, 46, 3095) and is usually described as having passion fruit and grapefruit character.

3-mercapto-3-methyl-butan-1-ol has been found in roasted coffee (W. Holscher, O.G. Vitzthum, H. Steinhart, *J. Agric. Food Chem.* 1992, 40, 655) and in Sauvignon blanc wine (T. Tominaga, A. Furrer, R. Henry, D. Dubourdieu, *Flavour Fragrance J.* 1998, 13, 159). The flavor description by Holscher et al. is sweet, soup-like.

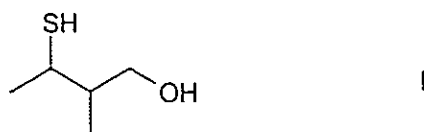
3-mercapto-2-methyl-propan-1-ol has been identified in red Bordeaux wine (P. Bouchilloux, P. Darriet, R. Henry, V. Lavigne-Cruège, D. Dubourdieu, *J. Agric. Food Chem.* 1998, 46, 3095) and has been described as broth, sweat-like.

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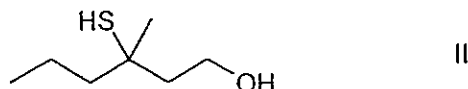
The German Offenlegungsschrift 2316456 describes γ -mercapto-alcohols and their formate and acetate esters as important odorants and flavorants that are useful for the preparation and modification of a broad range of flavor compositions. These compounds have been described as faint green, onion-like, sulfury and sweaty with a broad range of taste thresholds.

An object of the present invention is to provide new 3-mercapto-alkan-1-ols for use as flavor ingredients and/or as flavor enhancer.

Surprisingly, it has now been found that 2 new mercapto-alkanols, namely 3-mercapto-2-methyl-butan-1-ol of formula I

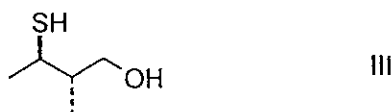


and 3-mercapto-3-methyl-hexan-1-ol of formula II



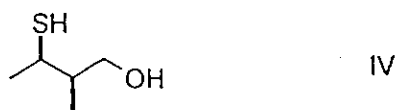
including all possible stereoisomers have very interesting flavor properties that are strongly dependent on the absolute and relative configuration of the compounds.

Especially interesting are the flavor properties of the two diastereoisomeric forms of 3-mercapto-2-methyl-butan-1-ol, namely (*u*)-3-mercapto-2-methyl-butan-1-ol of formula III



rel. configuration: *unlike*

and (*l*)-3-mercapto-2-methyl-butan-1-ol of formula IV.



rel. configuration: *like*

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It has been found that the (*u*)-3-mercapto-2-methyl-butan-1-ol enantiomers of formula III exhibit a strong onion-like note, with a surprisingly extreme low odor threshold value of 4 pg/l air. Due to this extremely strong aroma (*u*)-3-mercapto-2-methyl-butan-1-ol of formula III is a valuable flavor ingredient, and even at concentrations of down to 0,01 ppb in water, the flavor of these compounds can be recognized. It has been found that the enantiomers of formula III are useful to enhance the meaty, boiled meat character of a food product, especially meat products, at concentrations of 0.1 ppb to 1 ppb and to impart cooked vegetable and meaty notes to food products, especially soup products, at concentrations from 1ppb to 100 ppb.

It has been further found that the (*l*)-3-mercapto-2-methyl-butan-1-ol enantiomers of formula IV exhibit a herbaceous, onion-like, leeky and gassy character with a far higher threshold value of about 400 pg/l air as compared to the enantiomers of formula III. Surprisingly, it has been found that this compound is useful to enhance the typical natural, fruity character of exotic fruits at concentrations of 10 ppb to 50 ppm in a food product, preferably at concentrations in the range of 100 ppb to 5 ppm.

The compounds of formulae III and IV are not limited to any particular isomer; all possible enantiomers and all mixtures are thus included within the scope of the invention.

It has also been found that the two enantiomers of 3-mercapto-3-methyl-hexan-1-ol have quite different olfactory properties, the (*S*)-isomer exhibits herbaceous, agrestic and green notes whereas the (*R*)-isomer can be described as grapefruit/passion fruit, black currant and onion-like. Both enantiomers exhibit an extremely strong aroma, even at concentrations of down to 0,1 ppb in water, and are therefore valuable flavor ingredients. The (*S*)-3-mercapto-3-methyl-hexan-1-ol is useful to enhance the flavor properties of food products, especially the meaty, boiled meat character of meat products the cooked vegetable and meaty notes of soup products. The amount of flavorant needed to impart these flavor characteristics is depending on the food product to be flavored and is known to the person skilled in the art. Usually the concentrations are ranging from 0,1 ppb to 1 ppm, preferably from 1ppb to 100 ppb. The (*R*)-3-mercapto-3-methyl-hexan-1-ol is useful to enhance the typical natural, fruity character of exotic fruit flavors at concentrations of 10 ppb to 50 ppm in a food product, preferably at concentrations in the range of 100 ppb to 5 ppm.

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Depending on the desired flavor properties of the finished food or beverage product 3-mercapto-3-methyl-hexan-1-ol can be used in enantiomerically pure form or as mixtures thereof.

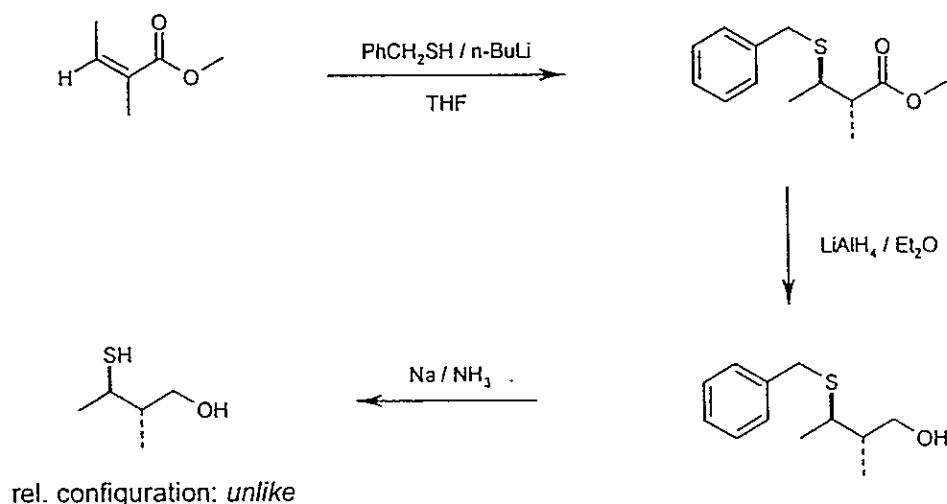
The 3-mercapto-alkanols of the present invention are useful for flavoring various products such as foods, beverages, chewing gums, oral hygiene products, and pharmaceuticals, but are especially favored for flavoring foods and beverages. The 3-mercapto-alkan-1-ols according to the present invention can be added directly to the product or preferably as flavor composition comprising usual additives that are well known to a person of skill in the art. The 3-mercapto-alkan-1-ols according to the present invention can also be used in flavoring compositions in order to enhance or modify existing flavors in order to provide a specific flavor impression. They may then be incorporated into the flavoring compositions exclusively or in combination with further flavor ingredients such as esters, aldehydes, ketones, alcohols, lactones, heterocycles as e.g. furans, pyridines, pyrazines, and other sulfur compounds as e.g. thiols, sulfides, disulfides and the like. These components can be combined in proportions normally used in the art for the preparation of flavoring and a person of skill in the art is well aware how to make use of these.

It may be desirable preparing the flavoring compositions according to the present invention by using carrier materials, e.g. gum arabic or maltodextrin, or solvents, e.g. ethanol, propyleneglycol, water or triacetin, yielding inter alia emulsions. By using carrier materials or solvents the desired physical form of the flavoring composition can be obtained. When the carrier materials build an emulsion, the flavoring composition may further contain emulsifiers such as mono- and diglycerides of fatty acids, and the like. The flavoring composition according to the invention may be used in spray-dried, liquid, encapsulated, emulsified or other form.

The 3-mercapto-alkan-1-ols of the present invention may be used solely or in combination with other flavor ingredients known by those skilled in the art. Thus, a flavor composition may contain one or more of the compounds according to the invention. The total content of one or more of these compounds is preferably in the range of 0,01 ppb to 50 ppm, preferably in the range of 1 ppb to 5 ppm, depending on the product which should be flavored.

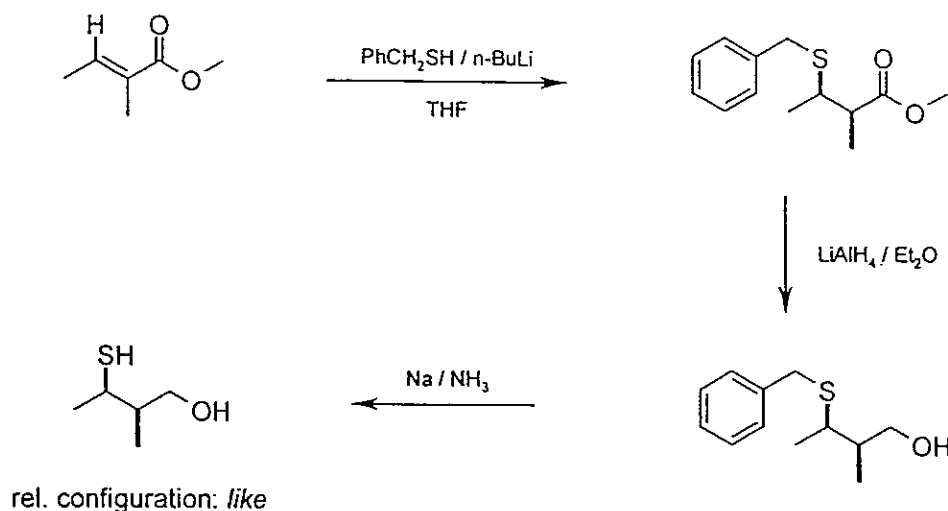
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A further object of the present invention is to provide a procedure for the stereospecific synthesis of the 2 diastereoisomeric forms of 3-mercapto-2-methyl-butan-1-ol of formula I, namely (*u*)-3-mercapto-2-methyl-butan-1-ol of formula III and (*l*)-3-mercapto-2-methyl-butan-1-ol of formula IV. The procedure for the preparation of (*u*)-3-mercapto-2-methyl-butan-1-ol comprises the condensation of benzyl mercaptan with angelic acid methyl ester, the reduction of the formed ester with lithium aluminum hydride and subsequent debenzylation with sodium in liquid ammonia. Using this procedure (*u*)-3-mercapto-2-methyl-butan-1-ol is obtained with a diastereoisomeric purity of >6:1. The isomerically enriched product can be used as such as flavorant to enhance the flavor properties of a food product, or it can be purified by chromatography to get diastereomerically pure (*u*)-3-mercapto-2-methyl-butan-1-ol, to be used as flavorant as described infra.



The procedure for the preparation of (*u*)-3-mercapto-2-methyl-butan-1-ol comprises the condensation of benzyl mercaptan with tiglic acid methyl ester, the reduction of the formed ester with lithium aluminum hydride and subsequent debenzylation with sodium in liquid ammonia. Using this procedure (*l*)-3-mercapto-2-methyl-butan-1-ol is obtained with a diastereoisomeric purity of >30:1. The isomerically enriched product can be used as such as flavorant to enhance the flavor properties of a food product, or it can be purified by chromatography to get diastereomerically pure (*l*)-3-mercapto-2-methyl-butan-1-ol, to be used as flavorant as described infra.

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The present invention is described further in the following examples showing specific embodiments, which are presented solely for the non-limiting purpose of further illustrating the invention.

Example 1

Preparation of (rac)-3-mercapto-3-methyl-hexan-1-ol

(a) (rac)-3-Methyl-2-hexenoic acid ethyl ester

35.5 g of NaH (0.8 mol, 60% in oil) was washed 2 times with hexane and suspended in 450 ml of THF. The suspension was warmed to 35° C and under stirring 222.2 g (0.98 mole) of triethyl phosphonoacetate was added such that the internal temperature remained between 35-45° C. Then 100 g (1.16 mol) of 2-pentanone was added over a period of 30 min., maintaining a temperature of 40-45°C, and stirring was continued for 1 h. The reaction mixture was cooled to room temperature and the layers were allowed to separate. The lower layer was taken up in 400 ml of H₂O and was extracted 3 times with 150 ml of hexane. The upper layer and the hexane layers were combined, dried over Na₂SO₄ and concentrated *in vacuo* and gave 172.4 g of a yellowish oil. Distillation at reduced pressure (42 mbar, 92° C) yielded 119.4 g (77%) of (rac)-3-methyl-2-hexenoic acid ethyl ester.

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NMR (CDCl₃): 0.93 (t, CH₃), 1.27 (t, CH₃), 1.50 (m, CH₂, isomer B), 1.51 (m, CH₂, isomer A), 1.89 (d, CH₃, isomer B), 2.10 (d, CH₂, isomer A), 2.16, (d, CH₃, isomer A), 2.60 (dd, CH₂, isomer B), 4.11 (q, CH₂, isomer B), 4.12 (q, CH₂, isomer A), 5.67 (q, CH) ppm.

MS: 156 (26, M⁺), 128(32), 111 (100), 95 (38), 82 (49), 69 (63), 55 (87), 41 (66), 29 (66).

IR (neat): 2962m, 2936m, 2874w, 1718s, 1649s, 1218s, 1149s, 1106m, 1040m.

(b) (*rac*)-3-benzylsulfanyl-3-methyl-hexanoic acid ethyl ester

A mixture of 62.1 g (0.5 mol) of benzyl mercaptan and 78.1 g (0.5 mol) of (*rac*)-3-methyl-2-hexenoic acid ethyl ester of step (a) in 100 ml of piperidine was heated at reflux until complete reaction was observed (48 h), cooled to room temperature. Then the excess of piperidine was distilled off at reduced pressure (0.04 mbar, 26-33° C). The residue, 96.5 g (68%) of (*rac*)-3-benzylsulfanyl-3-methyl-hexanoic acid ethyl ester, was of good purity and was directly used in the next step.

NMR (CDCl₃): 0.90 (t, CH₃), 1.29 (t, CH₃), 1.43 (s, CH₃), 1.40-1.65 (m, 2 CH₂), 2.61 (s, CH₂), 3.75 (s, CH₂), 4.16 (q, CH₂), 7.15-7.38 (m, 5 arom. H) ppm.

MS: 280 (3, M⁺), 235 (1), 157 (17), 122 (27), 91 (100), 83 (59), 45 (36), 29 (51).

IR (neat): 2960m, 2933m, 2872w, 1732s, 1453m, 1198m.

(c) (*rac*)-3-benzylsulfanyl-3-methyl-hexan-1-ol

At a temperature of 0° C to a suspension of 6.8 g (0.18 mol) of LiAlH₄ in 200 ml of Et₂O was slowly added 50.0 g (0.18 mol) of (*rac*)-3-benzylsulfanyl-3-methyl-hexanoic acid ethyl ester of step (b) under stirring such that the temperature did not exceed 10° C. Stirring was continued for 1 h and under cooling acetone and then 400 ml of a saturated NH₄Cl solution was slowly added. The reaction mixture was extracted 3 times with 200 ml of Et₂O, the combined organic layers were dried over Na₂SO₄ and concentrated *in vacuo*

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and gave 40.8 g of a yellowish oil. After drying in high vacuo (0.05 mbar/150° C) 32.5 g (75%) of (*rac*)-3-benzylsulfanyl-3-methyl-hexan-1-ol in form of a yellowish oil was obtained.

NMR (CDCl₃): 0.90 (t, CH₃), 1.30 (s, CH₃), 1.35-1.60 (m, 2 CH₂), 1.85 (m, CH₂), 2.40 (br., OH), 3.73 (s, CH₃), 3.82 (td, CH₂), 7.15-7.38 (m, 5 arom. H) ppm.

MS: 238 (4, M⁺), 114 (13), 97 (40), 91 (89), 55 (100), 41 (28).

IR (neat): 3357br, 2957s, 2931s, 2871m, 1453m, 1042m.

(d) (*rac*)-3-mercapto-3-methyl-hexan-1-ol

At a temperature of -78° C to a solution of 16.0 g (67.1 mmol) of (*rac*)-3-benzylsulfanyl-3-methyl-hexan-1-ol of step (c) in 200 ml of Et₂O was added from a cylinder about 200 ml of NH₃. Then pieces of Na (ca. 4.0 g) were added until the reaction mixture remained blue for more than 20 min. The blue colored mixture was allowed to warm up to room temperature overnight and EtOH was added until the blue color disappeared. The mixture was then acidified with about 2.7 M of HCl, and extracted 3 times with 150 ml of Et₂O. The combined organic layers were dried over Na₂SO₄ and concentrated *in vacuo*. Distillation of the crude product at reduced pressure (40 mbar/130° C) gave 11.2 g (73%) of (*rac*)-3-mercapto-3-methyl-hexan-1-ol in form of a colorless oil.

main flavor: passion fruit, black currant, green

NMR (CDCl₃): 0.94 (t, CH₃), 1.37 (s, CH₃), 1.38-1.62 (m, 2 CH₂), 1.70 (s, SH), 1.88 (m, CH₂), 2.30 (br., OH), 3.82 (td, CH₂) ppm.

MS: 148 (1, M⁺), 114 (12), 97 (25), 71 (37), 55 (100), 41 (68).

IR (neat): 3346br, 2959s, 2932s, 2872m, 1456m, 1046m.

Example 2Preparation of (S)-3-mercapto-3-methyl-hexan-1-ol(a) (*rac*)-3,5-Dinitro-benzoic acid 3-mercapto-3-methyl-hexyl ester

To a solution of 5.0 g (34 mmol) of (*rac*)-3-mercapto-3-methyl-hexan-1-ol in 20 ml of CCl₄ was added in portions 8.6 g (37 mmol) of 3,5-dinitrobenzoyl chloride. The mixture was stirred for 72 h, then 10 ml of a saturated NaHCO₃ solution were added, the organic layer was separated, washed with 15 ml of brine, dried over MgSO₄ and concentrated *in vacuo*. The residue was purified by flash-chromatography (silicagel, hexane/EtOAc 4:1) and gave 9.8 g (84%) of (*rac*)-3,5-dinitro-benzoic acid 3-mercapto-3-methyl-hexyl ester.

NMR (CDCl₃): 0.97 (t, CH₃), 1.44 (s, CH₃), 1.40-1.72 (m, 2 CH₂), 1.68 (s, SH), 2.12 (m, CH₂), 4.67 (t, CH₂), 9.15 (d, 2H), 9.24 (t, 1H) ppm.

MS: 342 (5, M⁺), 309 (2), 195 (9), 103 (12), 97 (95), 87 (25), 55 (100), 41 (21).

IR (neat): 3101m, 2961m, 2933m, 1732s, 1629m, 1547s, 1463m, 1345s, 1279s, 1168s.

(b) (1*S*,3*S*)- 3,5-Dinitro-benzoic acid 3-methyl-3-(4,7,7-trimethyl-3-oxo-2-oxa-bicyclo[2.2.1]heptane-1-carbonylsulfanyl)-hexyl ester

To a solution of 9.8 g (28.6 mmol) of (*rac*)-3,5-dinitro-benzoic acid 3-mercapto-3-methyl-hexyl ester of step (a) and 2.5 g (31.5 mmol) of pyridine in 80 ml of CCl₄ was added under stirring 6.82 g (31.5 mmol) of (-)-camphanic acid chloride. The mixture was heated at reflux temperature for 48 h. Another 1.86 g (0.3 eq.) of (-)-camphanic chloride and 0.68 g (0.3 eq.) of pyridine were added and stirring at reflux temperature was continued for 16 h. The mixture was cooled to room temperature, 50 ml of saturated NaHCO₃ solution was added and the layers were separated. The organic layer was washed with 40 ml saturated NaHCO₃ solution and 40 ml of H₂O, dried over MgSO₄ and concentrated *in vacuo* and gave 16.0 g of a yellow oil. Chromatography (silicagel, hexane/EtOAc 4:1) of the crude product yielded 10.0 g of an orange oil. Repeated crystallization from Et₂O in the refrigerator gave 1.84 g diastereomerically pure (1*S*,3*S*)-3,5-dinitro-benzoic acid 3-methyl-

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3-(4,7,7-trimethyl-3-oxo-2-oxa-bicyclo[2.2.1]heptane-1-carbonylsulfanyl)-hexyl ester. X-ray study of crystals grown from CH₃CN allowed the determination of the absolute configuration at C-3 to be *S*.

NMR (CDCl₃) : 0.99 (s, CH₃), 1.05 (s, CH₃), 1.10, (s, CH₃), 1.21 (t, CH₃), 1.35-2.05 (m, 7 H), 1.57 (s, CH₃), 2.42-2.55 (m, 3H), 4.58 (t, CH₂), 9.15 (d, 2H), 9.23 (t, 1H) ppm.

MS: 522 (0.1, M⁺), 492 (0.5), 309 (15), 214 (3), 195 (3), 55 (62).

IR (neat): 3104m, 2965s, 2934m, 2874m, 1795s, 1734s, 1659s, 1547s, 1463m, 1345s, 1279s, 1166s.

(c) (*S*)-3-mercapto-3-methyl-hexan-1-ol

To a suspension of 0.28 g (7.5 mmol) of LiAlH₄ in 10ml of Et₂O was added a solution of 1.3 g of (1*S*,3*S*)- 3,5-dinitro-benzoic acid 3-methyl-3-(4,7,7-trimethyl-3-oxo-2-oxa-bicyclo[2.2.1]heptane-1-carbonylsulfanyl)-hexyl ester of step (b) in 10 ml of THF. The reaction mixture was stirred at room temperature overnight, quenched with 20 ml of water and filtrated over Celite. The organic layer was separated, dried over MgSO₄ and concentrated *in vacuo*. The residue was distilled (bulb to bulb, 0.06 Torr, up to 190° C) and gave 100 mg (27%) of (*S*)-3-mercapto-3-methyl-hexan-1-ol in form of a colorless oil.

NMR (CDCl₃): 0.94 (t, CH₃), 1.37 (s, CH₃), 1.38-1.62 (m, 2 CH₂), 1.70 (s, SH), 1.88 (m, CH₂), 2.30 (br., OH), 3.82 (t, CH₂) ppm.

[α]_D²²: -2.5 (c = 0.8, CHCl₃)

main flavor: herbaceous, agrestic, green

Example 3Preparation of (*l*)-3-mercapto-2-methyl-butan-1-ol (racemic)(a) (*l*)-3-benzylsulfanyl-2-methyl-butyric acid methyl ester

At a temperature of 0° C to a solution of 13.0 ml of *n*-BuLi (1.6 M in hexane) in 500 ml of THF was added under stirring 236 ml (2.0 mol) of benzyl mercaptan. Then a solution of 23.6 g (0.2 mol) of tiglic acid methyl ester in 500 ml of THF was added. The reaction mixture was allowed to warm up to room temperature and stirring was continued for 3.5 h. The reaction mixture was quenched with 200 ml of a 5% NaOH solution and the organic layer was separated and dried over MgSO₄. THF and benzyl mercaptan were distilled off *in vacuo* (rotary evaporator, 10 mbar/60° C) and the residue was distilled (0.1 mbar, 110-118° C) and gave 40.8 g (85.7%) (*l*)-3-benzylsulfanyl-2-methyl-butyric acid methyl ester in form of a colorless oil having a diastereoisomeric purity of 98:2 (NMR).

NMR (CDCl₃): 1.22 (d, CH₃), 1.28 (d, CH₃), 2.57 (m, CH), 2.96 (m, CH), 3.64 (s, CH₃), 3.72 (s, CH₂), 7.15-7.35 (m, 5 arom. H) ppm.

MS: 238 (3, M⁺), 151 (3), 147 (15), 123 (27), 91 (100), 59 (18).

IR (neat): 3028w, 2977m, 2950m, 1736s, 1495m, 1453s, 1200m.

(b) (*l*)-3-benzylsulfanyl-2-methyl-butan-1-ol

At a temperature of 0° C to a suspension of 4.78 g (126 mmol) of LiAlH₄ in 150 ml of Et₂O was added a solution of 20.0 g (84 mmol) of (*l*)-3-benzylsulfanyl-2-methyl-butyric acid methyl ester of step (a) in 100 ml of Et₂O. The reaction mixture was allowed to warm up to room temperature, stirring was continued for 5 h. Then H₂O was slowly added until no more H₂ evolution was observed. The reaction mixture was filtrated over Celite, the organic layer was dried over MgSO₄ and concentrated *in vacuo*. Distillation of the crude product at reduced pressure (0.05 Torr/110° C) gave 15.5 g (87%) of (*l*)-3-benzylsulfanyl-2-methyl-butan-1-ol.

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NMR (CDCl₃): 0.89 (d, CH₃), 1.29 (d, CH₃), 1.60 (t, OH), 1.87 (m, CH), 2.84 (qd, CH), 3.37-3.68 (m, CH₂), 3.74 (d, CH₂), 7.18-7.38 (m, 5 arom. H) ppm.

MS: 210 (6, M⁺), 151 (7), 123 (9), 91 (100), 45 (17), 31 (8).

IR (neat): 3381br, 3028w, 2961s, 2921s, 2875s, 1494m, 1452s, 1029s.

(c) (*D*)-3-mercapto-2-methyl-butan-1-ol

About 200 ml of NH₃ were condensed from a cylinder into a cold flask at -78° C and small pieces of Na were added until a blue color persisted. Then under stirring 3.47 g (64 mmol) of (*D*)-3-benzylsulfanyl-2-methyl-butan-1-ol were added in small portions. Since the reaction mixture became colorless, the Na addition was continued until a blue color persisted again. Stirring at -78° C was continued for 1 h, then the mixture was quenched with saturated NH₄Cl solution until it became colorless, acidified with 100 ml 2N HCl and extracted with Et₂O. The combined organic layers were dried over MgSO₄ and concentrated *in vacuo*. The crude product was distilled at reduced pressure over a 10 cm Vigreux-column (0.15 Torr/60° C) and gave 5.8 g (86%) (*D*)-3-mercapto-2-methyl-butan-1-ol in form of a colorless oil having a diastereoisomeric purity of 40:1 (NMR).

NMR (CDCl₃): 0.90 (d, CH₃), 1.28 (d, SH), 1.37 (d, CH₃), 1.72 (s, OH), 1.86 (m, CH), 3.28 (m, CH), 3.60 (m, CH₂) ppm.

MS: 120 (12, M⁺), 102 (3), 86 (55), 71 (60), 61 (89), 45 (89), 41 (100), 31 (83).

IR (neat): 3356br, 2964s, 2926s, 2876s, 1450m, 1379m, 1039s.

main flavor: herbaceous, onion-like, leeky, gassy

Example 4Preparation of (*u*)-3-mercapto-2-methyl-butan-1-ol (racemic)(a) (*u*)-3-benzylsulfanyl-2-methyl-butyric acid methyl ester

At a temperature of 0° C to a solution of 13.0 ml of *n*-BuLi (1.6 M in hexane) in 500 ml of THF was added 236 ml (2.0 mol) of benzyl mercaptan. Then a solution of 23.6 g (0.2 mol) of angelic acid methyl ester in 500 ml of THF was added. The reaction mixture was stirred at 0° C for 3.5 h, quenched with 200 ml of a 5% NaOH solution. The organic layer was separated and dried over MgSO₄. THF and benzyl mercaptan were distilled off *in vacuo* (rotary evaporator, 10 mbar/60° C) and the residue was distilled (0.1 mbar, 104-130° C) and gave 28.2 g (59%) (*u*)-3-benzylsulfanyl-2-methyl-butyric acid methyl ester in form of a colorless oil having a diastereoisomeric purity of 9:1 (NMR).

NMR (CDCl₃): 1.18 (d, CH₃), 1.20 (d, CH₃), 2.65 (m, CH), 3.03 (m, CH), 3.66 (s, CH₃), 3.72 (s, CH₂), 7.15-7.35 (m, 5 arom. H) ppm.

MS: 238 (3, M⁺), 151 (2), 147 (12), 123 (22), 91 (100).

IR (neat): 3029w, 2975m, 1736s, 1495m, 1453s, 1199m.

(b) (*u*)-3-benzylsulfanyl-2-methyl-butan-1-ol

At a temperature of 0° C to a suspension of 4.78 g (126 mmol) of LiAlH₄ in 150 ml of Et₂O was added under stirring a solution of 20.0 g (84 mmol) of (*u*)-3-benzylsulfanyl-2-methyl-butyric acid methyl ester in 100 ml of Et₂O. The reaction mixture was allowed to warm up to room temperature and stirring was continued for 5 h. Then H₂O was slowly added until no more H₂ evolution was observed. The reaction mixture was filtrated over Celite, the organic layer was dried over MgSO₄ and concentrated *in vacuo*. Distillation of the crude product at reduced pressure (0.05 Torr/100° C) gave 14.7 g (83%) of (*u*)-3-benzylsulfanyl-2-methyl-butan-1-ol having a diastereoisomeric purity of 6.5:1 (NMR).

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NMR (CDCl₃): 0.95 (d, CH₃), 1.22 (d, CH₃), 1.73 (t, OH), 1.86 (m, CH), 2.78 (m, CH), 3.53 (m, CH₂), 3.74 (d, CH₂), 7.18-7.38 (m, 5 arom. H) ppm.

MS: 210 (6, M⁺), 151 (7), 123 (9), 91 (100), 45 (17).

IR (neat): 3377br, 3028w, 2963s, 2923s, 2875s, 1494m, 1452s, 1029s.

(c) (*u*)-3-benzylsulfanyl-2-methyl-butan-1-ol

About 200 ml of NH₃ were condensed into a flask at -78° C and small pieces of Na were added until a blue color persisted. Then under stirring 9.5 g (40 mmol) of (*u*)-3-benzylsulfanyl-2-methyl-butan-1-ol of step (b) were added in small portions. Since the reaction mixture became colorless, Na addition was continued until a blue color persisted again. Stirring at -78° C was continued for 1 h, the mixture was quenched with saturated NH₄Cl solution until it became colorless, acidified with 100 ml 2N HCl and extracted with Et₂O. The combined organic layers were dried over MgSO₄ and concentrated *in vacuo*. The crude product was distilled at reduced pressure over a 10 cm Vigreux-column (0.06 Torr/47° C) and gave 3.0 g (62%) (*u*)-3-mercapto-2-methyl-butan-1-ol in form of a colorless oil having a diastereoisomeric purity of 6.5:1.

NMR (CDCl₃): 1.00 (d, CH₃), 1.35 (d, CH₃), 1.51 (d, SH), 1.78 (m, CH), 1.97 (br, OH), 3.08 (m, CH), 3.65 (d, CH₂).

MS: 120 (13, M⁺), 102 (4), 86 (58), 71 (62), 61 (90), 45 (79), 41 (100), 31 (76).

IR (neat): 3353br, 2965s, 2928s, 2876s, 1449m, 1379m, 1034s.

main flavor: strong onion-like, brothy character

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Example 5Flavor tests in food

A meat base having the following composition (parts by weight), was prepared:

water	10
HVP	30
thiamin HCl	10
smoke extract	50
total	100

With this meat base the following bouillons were prepared:

Bouillon A (reference)

starting material: bouillon fat free

added thereto:

meat base	100 ppm
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Bouillon B

starting material: bouillon fat free

added thereto:

meat base	100 ppm
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(rac)-(u)-3-mercapto-2-methyl-butan-1-ol	1 ppb
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Bouillon C

starting material: bouillon fat free

added thereto:

meat base 100 ppm

(R)-3-mercapto-3-methyl-hexan-1-ol 1 ppb

The bouillons A and B have been compared in a blind test by an expert panel of 6 flavorists. The panel judged the bouillon B to have a fuller, more bouillon-like aroma with increased meaty and fatty notes.

The bouillons A and C have been compared in a blind test by an expert panel of 6 flavorists. The panel judged the bouillon C to have a fuller, sweeter, more bouillon-like aroma with increased chicken-meat, fatty and onion notes.

Thus, in both tests the present flavor components enhance the bouillon or meat character, respectively.

Example 6Flavor test in beverage

Flavoring compositions A and B having a passion fruit flavor were prepared using the following ingredients (parts by weight):

Ingredient	A	B
Hexyl butyrate	96	96
Ethyl hexanoate	82	82

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<i>cis</i> -3-Hexenol	86	86
Linalool	31	31
Hexanal	9	9
Citral	11	11
Methyl 2-octenoate	34	34
Furanol	48	48
Hexanoic acid	68	68
Orange oil	247	207
Ocimene	69	69
2-Methyl-heptanoic acid	27	27
2-Hexenoic acid	137	137
<i>cis</i> -3-Hexenyl acetate	55	55
(<i>rac</i>)-3-Mercapto-3-methyl-hexan-1-ol	—	40
total	1000	1000

The passion fruit flavoring compositions A and B have been added, at 2 drops per 100 ml beverage (about 200 mg/l), to a standard still beverage that was prepared by 1+5 dilution of a beverage syrup of the following composition (parts by weight):

Ingredient	
Sugar Syrup, 65 Bx	1033
Sodium benzoate	1
Trisodium citrate	2
Citric acid anhydrous, 50% w/w in water	30

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Water, cold filled up to 1000 ml

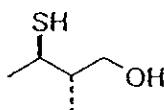
The thus prepared passion fruit drink AA containing the flavoring composition A and the passion fruit drink BB containing the flavoring composition B with about 5 ppm of a compound of the present invention, namely (*rac*)-3-mercapto-3-methyl-hexan-1-ol, have been evaluated in a blind test by an expert panel of 6 flavorists. The panel judged the passion fruit drink BB to have a more rounded off passion fruit flavor with typical exotic fruit character, having a greener, fresher and fruitier character than fruit drink AA.

While the invention has been illustrated and described with respect to illustrative embodiments and modes of practice, it will be apparent to those skilled in the art that various modifications and improvements may be made without departing from the scope and spirit of the invention. Accordingly, the invention is not be limited to the illustrative embodiments and modes or practice.

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Claims

1. 3-mercapto-2-methyl-butan-1-ol having the formula

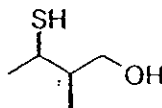


III

rel. configuration: *unlike*

and the enantiomer thereof.

2. 3-mercapto-2-methyl-butan-1-ol having the formula

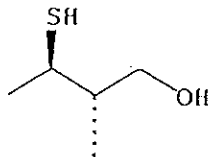


IV

rel. configuration: *like*

and the enantiomer thereof.

3. 3-mercapto-2-methyl-butan-1-ol enriched in a ratio of more than 6:1 in the diastereomer having the formula

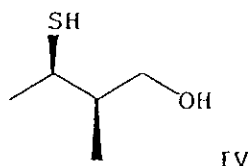


III

rel. configuration: *unlike*.

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4. 3-mercapto-2-methyl-butan-1-ol enriched in a ratio of more than 30:1 in the diastereomer having the formula



rel. configuration: *like*.

5. Use of a compound of any one of the claims 1 to 4 as flavorant.
6. A flavor composition containing at least one of the compounds of claims 1 to 4.
7. The flavor composition of claim 6 containing a stereoisomer of the compound of claim 1 or mixtures thereof.
8. The flavor composition of claim 6 containing a stereoisomer of the compound of claim 3 or mixtures thereof.
9. A flavor composition of any one of the claims 6 to 8 containing altogether one or more of the compounds in the range of about 0,01 ppb to 50 ppm.
10. A food or beverage product containing a flavor composition of any one of the claims 6 to 8.

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Abstract

FLAVOR COMPOUNDS

The present invention relates to 3-mercapto-2-methyl-butan-1-ol and 3-mercapto-3-methyl-hexan-1-ol including their stereoisomers, flavoring compositions and to food or beverage products flavored with at least one of these compounds.