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(71) Applicant: **GIVAUDAN SA** [CH/CH]; Chemin de la Parfumerie 5, CH-1214 Vernier (CH).

(72) Inventors: **DASTRUP, David Max**; 2330 Sunshine Place, Columbus, Ohio 43232 (US). **FLAMME, Eric**; 1116 McLaughlin Pl., Cincinnati, Ohio 45226 (US). **FURRER, Stefan Michael**; 1220 Forest Court, Cincinnati, Ohio 45215 (US).

(74) Agent: **SIMMONS, John**; Ueberlandstrasse 138, CH-8600 Duebendorf (CH).

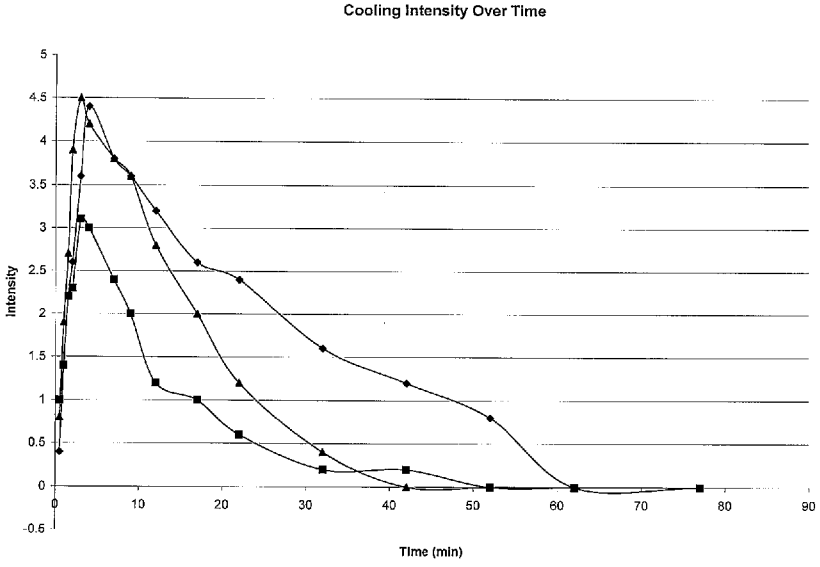
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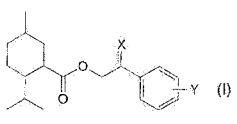
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[Continued on next page]

(54) Title: 3-SUBSTITUTED PARA-METHANE DERIVATIVES

Figure1





(I)

(57) Abstract: A compound formula (I) wherein the symbol represents a double bond when X is an oxygen atom or a single bond when X is a hydroxy] group, and Y represents a hydrogen atom or a substituent in the meta or para position, the substituent if present being hydroxyl, CN or -CH_2CN, useful as a cooling compound.

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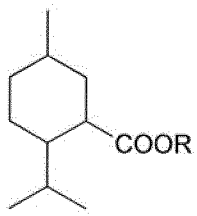
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3-SUBSTITUTED PARA-MENTHANE DERIVATIVES

The present disclosure is concerned with cooling compounds and their use in consumer product applications.

3-substituted p-menthane derivatives are known in the art, which have pronounced cooling activity, are of low volatility and have little or no odour. Principle among these derivatives is the class of menthane carboxamides.

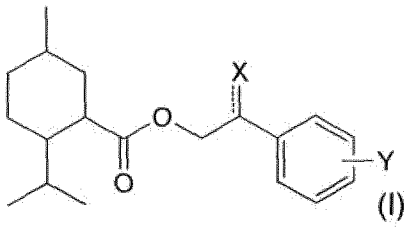
US patent 4,033,994 describes a series of 3-substituted p-methane derivatives of the general formula



wherein R can represent a variety of substituents including an aliphatic radical and an aryl radical with an hydroxyl substitutent in its 2 or 3 position relative to the ester group. The coolant properties of some of these molecules are described.

There remains a need to provide coolant compounds that have a pronounced and long lasting physiological cooling effect that have low or no odour.

In a first aspect, a compound is provided of the formula (I)



(I)

wherein

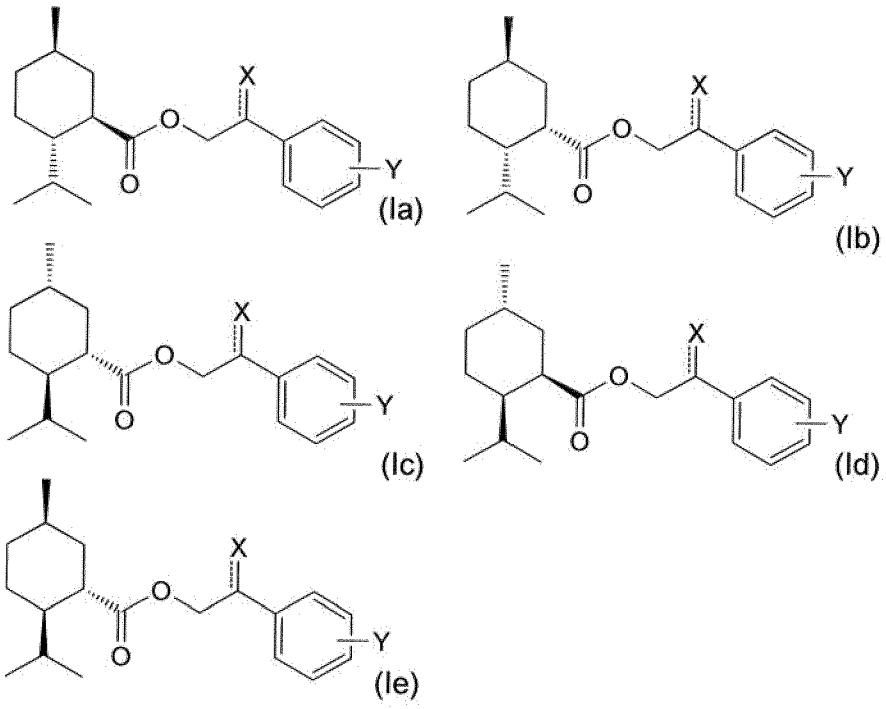
the symbol ------ represents a double bond when X is an oxygen atom or a single bond when X is a hydroxyl group, and Y represents a hydrogen atom or a substituent in the meta or para position, said substituent being selected from hydroxyl, CN or -CH_2CN.

Particular compounds of formula (I) include those wherein

the symbol ------ represents a double bond, X is an oxygen atom and Y is hydrogen;

the symbol ------ represents a single bond, X is a hydroxyl group and Y is a hydrogen atom, Y is a hydroxyl group at the meta position, or Y is CN or –CH_2CN at the para position.

In a particular embodiment the compound of the formula (I) may be represented by the formulae



wherein the symbols X, Y and ------ are as hereinabove defined.

In a particular embodiment, the symbol ------ is a single bond and X represents an hydroxyl group.

In a more particular embodiment, there is provided a compound of the formula (Ia), wherein the symbol ------ is a single bond and X represents an hydroxyl group. A a still more particular embodiment there is provided a compound of the formula (Ia), wherein the symbol ------ is a single bond and X represents an hydroxyl group and Y represents a hydrogen atom.

In another particular embodiment, there is provided a compound a compound of the formula (Ia), wherein the symbol ------ is a double bond, X represents an hydroxyl group and Y represents a hydrogen atom.

The skilled person will appreciate that the compounds of formula (I) or indeed (Ia) through (Ie) can exist in stereoisomeric forms. Accordingly, when reference is made herein to a compound of formula (I), or indeed (Ia) through (Ie), it should be understood that this may refer to either a single stereoisomer or a mixture of stereoisomers.

Compounds of formula I display a cooling effect that is long lasting compared to well known cooling agents such as WS3, as well as structurally related p-menthane derivatives substituted at the 3-position with ester functionality. This comparatively long-lasting cooling effect is illustrated in the examples, below.

The compounds of the present invention may be readily prepared according to conventional methods. One method of preparation is the esterification of p-menthane carboxylic acid with styrene oxide (2-phenyl oxirane) and a base, such as potassium carbonate. Further description of a synthetic route is set out in the examples below.

Compounds of formula (I) are practically odourless and flavourless, but have a long-lasting cooling effect. Due to this desirable organoleptic profile the compounds of formula (I) are suitable for use in all manner of consumer product applications. It may add desirable organoleptic properties to oral care and personal care products as well as in fragrance and flavour applications.

Accordingly, in another aspect there is provided a method to confer, enhance, improve or modify the organoleptic properties of a consumer product composition, which method comprises adding to said composition a compound of formula (I).

In another aspect, a consumer product composition is provided comprising a compound of formula (I).

In addition to a compound of formula (I), a consumer product composition may contain other ingredients such as other coolant materials, carrier materials, fragrance or flavour ingredients, or adjuvants useful in flavour compositions.

The term "carrier materials" as used herein refers to materials that are neutral or practically neutral from a coolant point of view, that is, the material does not significantly alter the coolant properties of a consumer product composition.

Carrier materials can include emulsifying systems, gums, polymers or encapsulating means. By "encapsulating means" is meant that a compound of formula (I) is contained within an encapsulating material, which protects and/or retains it and permits its release either gradually or completely. All known methods of encapsulation, may be used, for example, coacervation, spray drying and absorption into or onto a porous substrate. All possible encapsulation materials may also be used, for example, natural fibres, minerals of large surface area and polymeric materials.

The fragrance or flavour ingredients are ingredients that are used to impart a hedonic effect on consumer product compositions distinct from a cooling effect. For an ingredient to be considered as a fragrance ingredient, it must be recognized by a person skilled in the art as being able to impart or modify in a positive or pleasant way the odour of a composition, and not just as having an odor. Similarly, if the ingredient is a flavour ingredient, it is recognised by a person skilled in the art as being able to create, modify or enhance a flavour accord.

The nature and type of the fragrance or flavour ingredients present that may be employed 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 however, fragrance 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 perfuming 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 perfumery.

Specific examples of flavour ingredients may include but are not limited to natural flavors, artificial flavors, spices, seasonings, and the like. Illustrative flavour ingredients include synthetic flavor oils and flavoring aromatics and/or oils, oleoresins, essences, distillates, and extracts derived from plants, leaves, flowers, fruits, and so forth, and a combination comprising at least one of the foregoing.

Generally any flavoring or food additive such as those described in Chemicals Used in Food Processing, publication 1274, pages 63-258, by the National Academy of Sciences, can be used. This publication is incorporated herein by reference.

The term "adjuvant" as used herein, refers to an ingredient that affects the performance of a composition other than its hedonic performance. For example,

an adjuvant may be an ingredient that acts as an aid to processing a composition, or it may improve handling or storage of said composition or article. It might also be an ingredient that provides additional benefits such as imparting colour or texture to a composition. It might also be an ingredient that imparts light resistance or chemical stability to one or more ingredients contained in the composition. A detailed description of the nature and type of adjuvant commonly used in consumer product compositions cannot be exhaustive, but it has to be mentioned that said ingredients are well known to a person skilled in the art. Examples of adjuvants include solvents and co-solvents; surfactants and emulsifiers; viscosity and rheology modifiers; thickening and gelling agents; preservative materials; pigments, dyestuffs and colouring matters; extenders, fillers and reinforcing agents; stabilisers against the detrimental effects of heat and light, bulking agents, acidulants, buffering agents and antioxidants.

The nature and type of the ingredients of a particular consumer product composition 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 and the desired effect of said composition. In general however, the present consumer product compositions may include compositions or articles common in perfumery, namely perfumes, colognes or after-shave lotions, perfumed soaps, shower or bath salts, mousses, oils or gels, hygiene products or hair care products such as shampoos, body-care products, deodorants or antiperspirants, air fresheners and also cosmetic preparations, papers or wipes.

Consumer products may also include any solid or liquid composition that is consumed for at least one of nourishment and pleasure, or intended to be held in

the mouth for a period of time before being discarded. A broad list includes, but is not limited to, foodstuffs of all kinds, confectionery, baked goods, sweet goods, dairy products and beverages, and oral care products.

It may not be possible to simply admix a compound of the formula (I) with some consumer product compositions because of stability, compatibility or solubility issues with ingredients contained in said compositions. In such cases, it would be necessary to formulate the compound of formula (I) in such as way as to obviate or lessen said stability, incompatibility or solubility issues. This might include encapsulating the compound of formula (I) or employing other stability, compatibility or solubility adjuvants.

The proportions in which the compound of formula (I) can be incorporated into the various aforementioned compositions vary within a wide range of values. These values are dependent on the nature of the composition and on the desired organoleptic effect as well as the nature of the co-ingredients in a given composition.

Concentrations may vary widely within the limits of about 0.0003% to 1 % (3 ppm to 10000 ppm) by weight, based on the weight of consumer product composition into which it is incorporated.

The compound of formula (I) is particularly useful as coolants in personal care compositions.

Personal care compositions comprising the compound of the formula (I) can, depending on how they are formulated, be used, for example, as creams, gels, lotions, alcoholic and aqueous/alcoholic solutions, emulsions or stick preparations. Certain adjuvants and carrier materials for use in cosmetic or dermatological

compositions include mild surfactants, co-emulsifiers, super-fatting agents, pearlescent waxes, bodying agents, thickeners, polymers, silicone compounds, fats, waxes, stabilizers, biogenic active ingredients, deodorant active ingredients, anti-dandruff agents, film formers, swelling agents, hydrotropic agents, preservatives, insect repellants, tanning agents, artificial self-tanning agents (e.g. dihydroxyacetone), stabilizers, antioxidants, perfume oils, dyes, antimicrobial agents and the like.

Particular lipid phase adjuvants or carriers include: mineral oils, mineral waxes; oils, such as triglycerides of capric or of caprylic acid, and also natural oils, such as, for example, castor oil; fats, waxes and other natural and synthetic fatty substances, in certain embodiments esters of fatty acids with alcohols of low carbon number, e.g. with isopropanol, propylene glycol or glycerol, or esters of fatty alcohols with alkanoic acids of low carbon number or with fatty acids; alkyl benzoate; silicone oils, such as dimethylpolysiloxane, diethylpolysiloxane, diphenylpolysiloxane, and mixed forms thereof .

Particular aqueous phase adjuvants or carrier materials include alcohols, diols or polyols (lower alkyl), and ethers thereof, in certain embodiments ethanol, isopropanol, propylene glycol, glycerol, ethylene glycol-monoethyl or monobutyl ether, propylene glycol monomethyl, -monoethyl or monobutyl ether, diethylene glycol monomethyl or -monoethyl ether and analogous products, and also alcohols (lower alkyl), e.g. ethanol, 1,2-propanediol, glycerol, and, in particular, one or more thickeners which can be chosen from the group of silicon dioxide, aluminum silicates, polysaccharides and derivatives thereof, e.g. hyaluronic acid, xanthan gum, hydroxypropylmethylcellulose, particularly from the group of polyacrylates, in certain embodiments a polyacrylate from the group of Carbopol™ products, for

example, Carbopol grades 980, 981, 1382, 2984, 5984, in each case individually or in combination.

When used within cosmetics and toiletries, the compounds of the formula (I) can be used in any of the "Reported Product Categories" listed by the Cosmetic, Toiletries and Fragrance Association's 'International Cosmetic Ingredient Dictionary and Handbook', and with any one or more of the ingredients cited as being used for the reported product categories.

The reported product categories are: Aftershave lotions, Baby lotions, oils, powders and creams, Baby products miscellaneous, Baby shampoos, Basecoats and undercoats, Bath capsules, Bath oils, tablets and salts, Bath preparations miscellaneous, Bath soaps and detergents, Beard softeners, Blushers, Body and hand preparations, Bubble baths, Cleaning products, Colognes and toilet waters, Cuticle softeners, Dentifrices, Deodorants, Depilatories, Douches, Eye lotions, Eye makeup preparations miscellaneous, Eye makeup removers, Eye shadows, Eyebrow pencils, Eyeliners, Face and neck preparations, Face powders, Feminine hygiene deodorants, Foot powders and sprays, foundations, Fragrance preparations miscellaneous, Hair bleaches, Hair colour sprays, Hair colouring preparations miscellaneous, Hair conditioners, Hair dyes and colours, Hair lighteners with colour, Hair preparations, Hair rinses, Hair shampoos, Hair sprays, Hair straighteners, Hair tints, Hair wave sets, Indoor tanning preparations, Leg and body paints, Lipsticks, Makeup bases, Makeup fixatives, Makeup preparations, Manicuring preparations miscellaneous, Mascara, Men's talcum, Moisturising preparations, Mouthwashes and breath fresheners, Nail creams and lotions, Nail extenders, Nail polish and enamel removers, Nail polish and enamels, Night skin care preparations, Oral hygiene products miscellaneous, Paste masks, Perfumes,

Permanent waves, Personal cleanliness products miscellaneous, Powders, Preshave lotions, Rouges, Sachets, Shampoos, Shaving cream, Shaving preparations miscellaneous, Shaving soap, Skin care preparations miscellaneous, Skin fresheners, Suntan gels, creams and liquids, Suntan preparations miscellaneous, after-sun preparations, Tonics, dressings and other hair grooming aids.

In the preparation of the abovementioned product categories, there may be used all or any of the standard ingredients typically found in such products, used in art-recognised quantities. Examples of such ingredients include (but are by no means limited to) solvents and co-solvents; surfactants and emulsifiers; viscosity and rheology modifiers; thickening and gelling agents; preservative materials such as fungicides and bactericides; pigments, dyestuffs and colouring matters; extenders, fillers and reinforcing agents; stabilisers against the detrimental effects of heat and light. Other suitable and desirable additives are described in standard texts, such as "Handbook of Industrial Chemical Additives", ed. M. and I. Ash, 2nd Ed., (Synapse 2000).

Further formulation details useful in association with the compound of formula (I) may be found in standard texts, for example, "Handbook of Cosmetic Science and Technology", ed. Pays, Barel & Maibach, 2nd Ed. (Dekker, 2005).

The compounds of formula (I) are particularly useful as coolants in oral care compositions.

By "oral care composition" is meant any composition applied to the oral cavity for the purposes of cleaning, freshening, healing, deodorising the cavity or any part thereof. Such compositions include, but are not limited to, tooth pastes, tooth gels, tooth powders, tooth whitening products, mouthwashes, lozenges, dental

floss, tooth picks, anti-plaque and anti-gingivitis compositions, throat lozenges, throat drops, inflammatory compositions, compositions for treatment of nasal symptoms, cold symptoms and upper gastrointestinal tract distress, compositions for cold relief, for alleviating discomfort of hot flash, gargle compositions, breath-freshening sprays, tooth polishes, denture adhesives and mouth rinses.

Oral care products utilising the compound of formula (I) may be prepared by blending with one or more of the conventional ingredients normally associated with such products, in standard quantities. Examples of such ingredients include, but are not limited to, L-Menthol, Mentha Arvensis, Mentha Piperita, Mentha Spicata, Mentha Cardiaca, Synthetic Mints, Anethole, Methyl Salicylate, Eucalyptol, Cinnamic Aldehyde, Eugenol, Calcium Carbonate, Silica (Precipitates & Xerogels), Dicalcium Phosphate, Alumina, Sodium Lauryl Sulphate, Betaine, Glycerine, Sorbitol, Water, Saccharin, Sodium Cyclamate, Aspartame, Xylitol, Sodium Carboymethyl Cellulose, Methyl Cellulose, Sodium Carageenate, Xanthan Gum, Polyvinyl Pyrrolidone, Sodium Tripolyphosphate, Ethyl Alcohol, Sodium Fluoride, Sodium Monofluorophosphate, Stannous Fluoride, Potassium Citrate, Potassium Chloride, Potassium Nitrate, Strontium Acetate, Strontium Chloride, Sodium Tripolyphosphate, Cetyl Pyridinium Chloride, Hexetidine, Sanguinarine, Triclosan, Chlorhexidine, Zinc Citrate, Zinc Sulphate, Zinc Chloride, Calcium Glycerophosphate, Sodium Bicarbonate, Tetra Sodium Pyrophosphate, Tetra Potassium Pyrophosphate.

Oral care compositions comprising a compound of the formula (I) can, depending on their formulation, be used, for example, as creams, gels, lotions, alcoholic and aqueous/alcoholic solutions, emulsions or stick preparations. Certain adjuvants and carrier materials for use in oral care compositions include mild surfactants, co-

emulsifiers, super-fatting agents, pearlescent waxes, bodying agents, thickeners, polymers, silicone compounds, fats, waxes, stabilizers, biogenic active ingredients, deodorant active ingredients, anti-dandruff agents, film formers, swelling agents, hydrotropic agents, preservatives, insect repellants, tanning agents, artificial self-tanning agents (e.g. dihydroxyacetone), stabilizers, antioxidants, perfume oils, dyes, antimicrobial agents and the like.

The amounts of oral care adjuvants and carrier materials, which can be used in each case can be determined easily by the person skilled in the art by simple trial and error, depending on the nature of the product in question.

Particular lipid phase adjuvants or carriers include: mineral oils, mineral waxes; oils, such as triglycerides of capric or of caprylic acid, and also natural oils, such as, for example, castor oil; fats, waxes and other natural and synthetic fatty substances, in certain embodiments esters of fatty acids with alcohols of low carbon number, e.g. with isopropanol, propylene glycol or glycerol, or esters of fatty alcohols with alkanoic acids of low carbon number or with fatty acids; alkyl benzoate; silicone oils, such as dimethylpolysiloxane, diethylpolysiloxane, diphenylpolysiloxane, and mixed forms thereof.

Particular aqueous phase adjuvants or carrier materials include alcohols, diols or polyols (lower alkyl), and ethers thereof, in certain embodiments ethanol, isopropanol, propylene glycol, glycerol, ethylene glycol-monoethyl or monobutyl ether, propylene glycol monomethyl, -monoethyl or monobutyl ether, diethylene glycol monomethyl or -monoethyl ether and analogous products, and also alcohols (lower alkyl), e.g. ethanol, 1,2-propanediol, glycerol, and, in particular, one or more thickeners which can advantageously be chosen from the group of silicon dioxide, aluminum silicates, polysaccharides and derivatives thereof, e.g. hyaluronic acid,

xanthan gum, hydroxypropylmethylcellulose, particularly advantageously from the group of polyacrylates, in certain embodiments a polyacrylate from the group of Carbopol™ products, for example, Carbopol grades 980, 981, 1382, 2984, 5984, in each case individually or in combination.

In the preparation of the abovementioned oral care compositions, there may be used all or any of the standard ingredients found in such products, used in art-recognised quantities. Examples of such ingredients include (but are by no means limited to) solvents and co-solvents; surfactants and emulsifiers; viscosity and rheology modifiers; thickening and gelling agents; preservative materials such as fungicides and bactericides; pigments, dyestuffs and colouring matters; extenders, fillers and reinforcing agents; stabilisers against the detrimental effects of heat and light. Other suitable and desirable additives are described in standard texts, such as "Handbook of Industrial Chemical Additives", ed. M. and I. Ash, 2nd Ed., (Synapse 2000)

The compounds of formula (I) are particularly useful as a coolant in food applications.

The compounds of formula (I) are useful in all manner of consumable compositions. By "consumable compositions" is meant any solid or liquid composition that is consumed for at least one of nourishment and pleasure. A broad general list includes, but is not limited to, foodstuffs of all kinds, confectionery, baked goods, sweet goods, dairy products and beverages. More specific examples follow:

The term "confectionery" includes, but is not limited to:

chewing gum (which includes sugarized gum, sugar-free gum, functional gum and bubble gum), centerfill confections, chocolate and other chocolate confectionery, medicated confectionery , lozenges, tablets, pastilles, mints, standard mints, power mints, chewy candies, hard candies, boiled candies, breath and other oral care films or strips, candy canes, lollipops, gummies, jellies, fudge, caramel, hard and soft panned goods, toffee, taffy, liquorice, gelatin candies, gum drops, jelly beans, nougats, fondants, or combinations of one or more of these, or edible compositions incorporating one or more of these.

The confectionery compositions can be incorporated into an otherwise conventional hard or soft confectionery format using standard techniques and equipment known to those of ordinary skill in the art. The confectionery compositions can also be center filled and/or coated with hard, soft, or particulate coatings.

The term "baked goods" includes, but is not limited to:
alfajores, bread, packaged/industrial bread, unpackaged/artisanal bread, pastries, cakes, packaged/industrial cakes, unpackaged/artisanal cakes, cookies, chocolate coated biscuits, sandwich biscuits, filled biscuits, savory biscuits and crackers, bread substitutes,

The term "sweet goods" includes, but is not limited to:
breakfast cereals, ready-to-eat ("rte") cereals, family breakfast cereals, flakes, muesli, other rte cereals, children's breakfast cereals, hot cereals.

The term "dairy products" includes, but is not limited to:
ice cream, impulse ice cream, single portion dairy ice cream, single portion water ice cream, multi-pack dairy ice cream, multi-pack water ice cream, take-home ice

cream, take-home dairy ice cream, ice cream desserts, bulk ice cream, take-home water ice cream, frozen yoghurt, artisanal ice cream, dairy products, milk, fresh/pasteurized milk, full fat fresh/pasteurized milk, semi skimmed fresh/pasteurized milk, long-life/uht milk, full fat long life/uht milk, semi skimmed long life/uht milk, fat-free long life/uht milk, goat milk, condensed/evaporated milk, plain condensed/evaporated milk, flavored, functional and other condensed milk, flavored milk drinks, dairy only flavored milk drinks, flavored milk drinks with fruit juice, soy milk, sour milk drinks, fermented dairy drinks, coffee whiteners, powder milk, flavored powder milk drinks, cream, yoghurt, plain/natural yoghurt, flavored yoghurt, fruited yoghurt, probiotic yoghurt, drinking yoghurt, regular drinking yoghurt, probiotic drinking yoghurt, chilled and shelf-stable desserts, dairy-based desserts, soy-based desserts,

Other foodstuff includes, but is not limited to:

chilled snacks, sweet and savory snacks, fruit snacks, chips/crisps, extruded snacks, tortilla/corn chips, popcorn, pretzels, nuts, other sweet and savory snacks, snack bars, granola bars, breakfast bars, energy bars, fruit bars, other snack bars, meal replacement products, slimming products, convalescence drinks, ready meals, canned ready meals, frozen ready meals, dried ready meals, chilled ready meals, dinner mixes, frozen pizza, chilled pizza, soup, canned soup, dehydrated soup, instant soup, chilled soup, uht soup, frozen soup, pasta, canned pasta, dried pasta, chilled/fresh pasta, noodles, plain noodles, instant noodles, cups/bowl instant noodles, pouch instant noodles, chilled noodles, snack noodles, dried food, dessert mixes, sauces, dressings and condiments, herbs and spices, spreads, jams and preserves, honey, chocolate spreads, nut-based spreads, and yeast-based spreads.

The term "beverage" as used herein means any drinkable liquid or semi-liquid, including for example:
flavored water, soft drinks, fruit drinks, coffee-based drinks, tea-based drinks, juice-based drinks (includes fruit and vegetable), milk-based drinks, gel drinks, carbonated or non-carbonated drinks, powdered drinks, alcoholic or non-alcoholic drinks.

In the preparation of the abovementioned food products, there may be used all or any of the standard ingredients found in such products, used in art-recognised quantities. Examples of such ingredients include (but are by no means limited to) solvents and co-solvents; surfactants and emulsifiers; viscosity and rheology modifiers; thickening and gelling agents; preservative materials; pigments, dyestuffs and colouring matters; extenders, fillers and reinforcing agents; stabilisers against the detrimental effects of heat and light, bulking agents, flavoring and flavor-enhancing agents, warming agents, breath fresheners, mouth moisteners, coloring agents, acidulants, buffering agents, antioxidants, sweetening agents and sensates, including materials that add tingling, numbing and warming effects.

Specific examples of sweetening agents include, but are not limited to:
sugar sweeteners (saccharide sweeteners), sugarless sweeteners, high-intensity sweeteners, or a combination of at least two of the foregoing sweetening agents.

Suitable bulking agents may include mineral adjuvants, which may serve as fillers and textural agents. Suitable mineral adjuvants include calcium carbonate, magnesium carbonate, alumina, aluminum hydroxide, aluminum silicate, talc, tricalcium phosphate, tricalcium phosphate and the like, which can serve as fillers and textural agents.

Additional bulking agents (carriers, extenders) suitable for use include sweetening agents such as monosaccharides, disaccharides, polysaccharides, sugar alcohols, polydextrose, and maltodextrins; minerals, such as calcium carbonate, talc, titanium dioxide, dicalcium phosphate; and combinations thereof.

Fillers modify the texture and aid processing. Examples of such fillers include magnesium and aluminum silicates, clay, alumina, talc, titanium oxide, cellulose polymers, and the like.

Specific examples of flavouring agents include, but are not limited to:
natural flavors, artificial flavors, spices, seasonings, and the like. Illustrative flavoring agents include synthetic flavor oils and flavoring aromatics and/or oils, oleoresins, essences, distillates, and extracts derived from plants, leaves, flowers, fruits, and so forth, and a combination comprising at least one of the foregoing.

Illustrative flavor oils include spearmint oil, cinnamon oil, oil of wintergreen (methyl salicylate), peppermint oil, Japanese mint oil, clove oil, bay oil, anise oil, eucalyptus oil, thyme oil, cedar leaf oil, oil of nutmeg, allspice, oil of sage, mace, oil of bitter almonds, and cassia oil; useful flavoring agents include artificial, natural and synthetic fruit flavors such as vanilla, and citrus oils including lemon, orange, lime, grapefruit, yazu, sudachi, and fruit essences including apple, pear, peach, grape, blueberry, strawberry, raspberry, cherry, plum, prune, raisin, cola, guarana, neroli, pineapple, apricot, banana, melon, apricot, ume, cherry, raspberry, blackberry, tropical fruit, mango, mangosteen, pomegranate, papaya and so forth. Additional illustrative flavors imparted by a flavoring agent include a milk flavor, a butter flavor, a cheese flavor, a cream flavor, and a yogurt flavor; a vanilla flavor; tea or coffee flavors, such as a green tea flavor, an oolong tea flavor, a tea flavor, a cocoa flavor, a chocolate flavor, and a coffee flavor; mint flavors, such as a

peppermint flavor, a spearmint flavor, and a Japanese mint flavor; spicy flavors, such as an asafetida flavor, an ajowan flavor, an anise flavor, an angelica flavor, a fennel flavor, an allspice flavor, a cinnamon flavor, a chamomile flavor, a mustard flavor, a cardamom flavor, a caraway flavor, a cumin flavor, a clove flavor, a pepper flavor, a coriander flavor, a sassafras flavor, a savory flavor, a Zanthoxyli Fructus flavor, a perilla flavor, a juniper berry flavor, a ginger flavor, a star anise flavor, a horseradish flavor, a thyme flavor, a tarragon flavor, a dill flavor, a capsicum flavor, a nutmeg flavor, a basil flavor, a marjoram flavor, a rosemary flavor, a bayleaf flavor, and a wasabi (Japanese horseradish) flavor; a nut flavor such as an almond flavor, a hazelnut flavor, a macadamia nut flavor, a peanut flavor, a pecan flavor, a pistachio flavor, and a walnut flavor; alcoholic flavors, such as a wine flavor, a whisky flavor, a brandy flavor, a rum flavor, a gin flavor, and a liqueur flavor; floral flavors; and vegetable flavors, such as an onion flavor, a garlic flavor, a cabbage flavor, a carrot flavor, a celery flavor, mushroom flavor, and a tomato flavor.

In some embodiments, other flavoring agents include aldehydes and esters such as cinnamyl acetate, cinnamaldehyde, citral diethylacetal, dihydrocarvyl acetate, eugenyl 49 formate, p-methylamisol, and so forth can be used. Further examples of aldehyde flavorings include acetaldehyde (apple), benzaldehyde (cherry, almond), anisic aldehyde (licorice, anise), cinnamic aldehyde (cinnamon), citral, i.e., alpha-citral (lemon, lime), neral, i.e., beta-citral (lemon, lime), decanal (orange, lemon), ethyl vanillin (vanilla, cream), heliotrope, i.e., piperonal (vanilla, cream), vanillin (vanilla, cream), alpha-amyl cinnamaldehyde (spicy fruity flavors), butyraldehyde (butter, cheese), valeraldehyde (butter, cheese), citronellal (modifies, many types), decanal (citrus fruits), aldehyde C-8 (citrus fruits), aldehyde C-9 (citrus fruits), aldehyde C- 12 (citrus fruits), 2-ethyl butyraldehyde (berry fruits),

hexenal, i.e., trans-2 (berry fruits), tolyl aldehyde (cherry, almond), veratraldehyde (vanilla), 2,6-dimethyl-5-heptenal, i.e., melonal (melon), 2,6-dimethyloctanal (green fruit), and 2-dodecenal (citrus, mandarin), and the like. Generally any flavoring or food additive such as those described in Chemicals Used in Food Processing, publication 1274, pages 63-258, by the National Academy of Sciences, can be used. This publication is incorporated herein by reference.

Some of these additives may serve more than one purpose. For example, a sweetener, e.g., sucrose, sorbitol or other sugar alcohol, or combinations of the foregoing sweeteners, may also function as a bulking agent. A combination comprising at least one of the foregoing additives is often used.

There may additionally be present nutraceuticals and medicaments.

Suitable nutraceuticals may include herbs and botanicals such as aloe, bilberry, bloodroot, calendula, capsicum, chamomile, cat's claw, echinacea, garlic, ginger, ginkgo, goldenseal, various ginseng, green tea, guarana, kava kava, lutein, nettle, passionflower, rosemary, saw palmetto, St. John's wort, thyme, and valerian. Also included are mineral supplements such as calcium, copper, iodine, iron, magnesium, manganese, molybdenum, phosphorous, zinc, and selenium. Other nutraceuticals may include fructooligosaccharides, glucosamine, grapeseed extract, cola extract, guarana, ephedra, inulin, phytosterols, phytochemicals, catechins, epicatechin, epicatechin gallate, epigallocatechin, epigallocatechin gallate, isoflavones, lecithin, lycopene, oligofructose, polyphenols, flavanoids, flavanols, flavonols, and psyllium as well as weight loss agents such as chromium picolinate and phenylpropanolamine. Illustrative vitamins and co-enzymes include water or fat soluble vitamins such as thiamin, riboflavin, nicotinic acid, pyridoxine, pantothenic acid, biotin, folic acid, flavin, choline, inositol and para-aminobenzoic

acid, carnitine, vitamin C, vitamin D and its analogs, vitamin A and the carotenoids, retinoic acid, vitamin E, vitamin K, vitamin B6, and vitamin B12. Combinations comprising at least one of the foregoing nutraceuticals may be used.

Suitable medicaments may include oral care agents, throat care agents, allergy relief agents, and general medical care agents. General medical care agents may include antihistamines, decongestants (sympathomimetics), antitussives (cough suppressants), antiinflammatories, homeopathic agents, expectorants, anesthetics, demulcents, analgesics, anticholinergics, throat- soothing agents, antibacterial agents, antiviral agents, antifungal agents, antacids, antinauseants, chemotherapeutics, diuretics, psychotherapeutic agents, cardiovascular agents, various alkaloids, laxatives, appetite suppressants, ACE-inhibitors, anti-asthmatics, anti-cholesterolemics, antidepressants, anti-diarrhea preparations, anti-hypertensives, anti-lipid agents, acne drugs, amino acid preparations, anti-uricemic drugs, anabolic preparations, appetite stimulants, bone metabolism regulators, contraceptives, endometriosis management agents, enzymes, erectile dysfunction therapies such as sildenafil citrate, fertility agents, gastrointestinal agents, homeopathic remedies, hormones, motion sickness treatments, muscle relaxants, osteoporosis preparations, oxytocics, parasympatholytics, parasympathomimetics, prostaglandins, respiratory agents, sedatives, smoking cessation aids such as bromocriptine or nicotine, tremor preparations, urinary tract agents, anti-ulcer agents, anti-emetics, hyper- and hypoglycemic agents, thyroid and anti-thyroid preparations, terine relaxants, erythropoietic drugs, mucolytics, DNA and genetic modifying drugs, and nutritional supplements, including nutraceuticals, micronutrients, vitamins and co-enzymes. The pharmaceutically acceptable salts and prodrugs of the medicaments are also included unless specified otherwise. Some of these medicaments may serve more than one purpose. Combinations of

the foregoing types of optional medicaments can be used. Two or more medicaments that have activity against the same or different symptoms can be used together in a combination.

Other suitable and desirable additives are described in standard texts, such as "Handbook of Industrial Chemical Additives", ed. M. and I. Ash, 2nd Ed., (Synapse 2000).

With respect to chewing gum compositions in particular, suitable components include in addition to a water-insoluble gum base portion, a water soluble bulk portion and various additives. The water soluble portion may include sweetening agents, bulking agents, softening agents and/or plasticizers, waxes, emulsifiers, thickening agents, flavor enhancing agents, warming agents, breath fresheners, mouth moisteners, acidulants, coloring agents, buffering agents, antioxidants, nutraceuticals, medicaments and other conventional chewing gum additives that provide desired attributes. Other conventional chewing gum additives known to one having ordinary skill in the art may also be used in the water soluble bulk portion.

Softeners and plasticizers may be used to provide a variety of desirable textures and consistency properties. Suitable plasticizers and softeners may include lanolin, palmitic acid, oleic acid, stearic acid, sodium stearate, potassium stearate, glyceryl triacetate, glyceryl lecithin, glyceryl monostearate, propylene glycol monostearate, acetylated monoglyceride, glycerine, and a combination comprising at least one of the foregoing. Because of the low molecular weights of these softeners and plasticizers, they are able to penetrate the fundamental structure of the gum base, making it plastic and less viscous.

Waxes may be used in the gum base to soften the elastomer, improve the elasticity of the gum base, and obtain a variety of desirable textures and consistency properties. Suitable waxes may include natural and synthetic waxes, hydrogenated vegetable oils, petroleum waxes such as polyurethane waxes, polyethylene waxes, paraffin waxes, microcrystalline waxes, fatty waxes, sorbitan monostearate, tallow, and propylene glycol. Low melting waxes may be used in the gum compositions. These waxes typically have a melting point below about 60°C, and specifically about 45 to about 55°C. High melting waxes may also be used in the gum base. Such high melting waxes include beeswax, vegetable wax, candelilla wax, camauba wax, most petroleum waxes, and the like, and combinations thereof.

Suitable emulsifiers include distilled monoglycerides, acetic acid esters of mono and diglycerides, citric acid esters of mono and diglycerides, lactic acid esters of mono and diglycerides, mono and diglycerides, polyglycerol esters of fatty acids, ceteareth-20, polyglycerol polyricinoleate, propylene glycol esters of fatty acids, polyglyceryl laurate, glyceryl cocoate, gum arabic, acacia gum, sorbitan monostearates, sorbitan tristearates, sorbitan monolaurate, sorbitan monooleate, sodium stearoyl lactylates, calcium stearoyl lactylates, diacetyl tartaric acid esters of mono- and diglycerides, glyceryl tricaprylate-caprate / medium chain triglycerides, glyceryl dioleate, glyceryl oleate, glyceryl lacto esters of fatty acids, glyceryl lacto palmitate, glyceryl stearate, glyceryl laurate, glycerlyl di laurate, glyceryl monoricinoleate, triglyceryl monostearate, hexaglyceryl distearate, decaglyceryl monostearate, decaglyceryl dipalmitate, decaglyceryl monooleate, polyglyceryl 10 hexaoleate, medium chain triglycerides, caprylic/capric triglyceride, propylene glycol monostearate, polysorbate 20, polysorbate 40, polysorbate 60, polysorbate 80, polysorbate 65, hexylglyceryl distearate, triglyceryl monostearate, tweens, spans, stearoyl lactylates, calcium stearoyl-2- lactylate, sodium stearoyl-2-lactylate lecithin,

ammonium phosphatide, sucrose esters of fatty acids, sucroglycerides, propane-1,2-diol esters of fatty acids, and combinations comprising at least one of the foregoing.

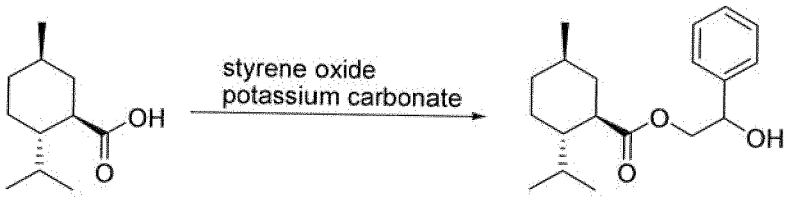
Suitable thickening agents include cellulose ethers (e.g., hydroxyethyl cellulose, hydroxypropylmethyl cellulose, or hydroxypropyl cellulose), methylcellulose, carboxymethylcellulose, and combinations thereof. Additional polymers useful as thickeners include carbomer, polyvinyl pyrrolidone, polyvinyl alcohol, sodium alginate, polyethylene glycol, natural gums like xanthan gum, tragacantha, guar gum, acacia gum, arabic gum, water-dispersible polyacrylates like polyacrylic acid, methyl methacrylate copolymer, and carboxyvinyl copolymers.

A chewing gum composition may additionally contain bulking agents and fillers, nutraceuticals, medicaments and flavoring agents, as hereinabove described.

The chewing gum composition may be coated or compressed, and be in the form of slabs, sticks, pellets, cubes, trapezoids, rectangles, or balls, and they may be layered. The compositions of the different forms of the gum compositions will be similar but may vary with regard to the ratios of the ingredients. Center-filled gum is another common gum form, the center-fill is typically an aqueous liquid or gel, which is injected into the center of the gum during processing. The center-filled gum may also be optionally coated and may be prepared in various forms, such as in the form of a lollipop

There now follows a series of examples that serve to illustrate, but not limit, the invention.

Example 1

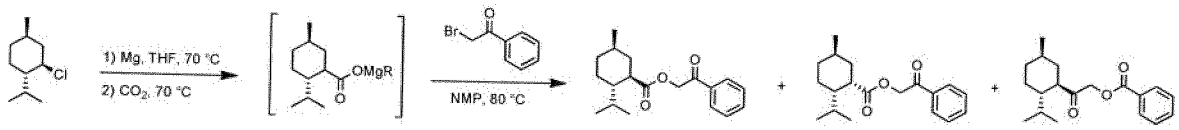


(1R,2S,5R)-2-hydroxy-2-phenylethyl2-isopropyl-5methylcyclohexanecarboxylate: Menthane carboxylic acid (15 g, 81 mmol), 2-phenyl oxirane (6.5 g, 54 mmol), and potassium carbonate (11.25 g, 81) were added to 150 ml of DMF and heated to 90 C with stirring for 20 hours. The reaction was cooled and diluted with water and extracted several times with MTBE. The organic layer was washed with water, 1 M NaOH , and saturated sodium bicarbonate, and brine. The organic layer was dried over sodium sulfate.. The crude oil was purified by silica gel chromatography using hexanes and MTBE. Isolate 9.7 grams of (1R,2S,5R)-2-hydroxy-2-phenylethyl2-isopropyl-5-methyl-cyclohexanecarboxylate as major isomer. Major isomer is 50-50 mixture of epimers around benzyl alcohol. ^{1}H NMR ($CDCl_3$) δ 7.43-7.27 (m, 5H), 4.97-4.92 (m, 1H), 4.35-4.27 (m, 1H), 4.24-4.14 (m, 1H), 2.54-2.52 (m, 1H), 2.38-2.28 (m, 1H), 1.87-1.78 (m, 1H), 1.77-1.62 (m., 2H), 1.61-1.45 (m, 2H), 1.44-1.28 (m, 1H), 1.23-1.13 (m, 1H), 1.12-0.94 (m, 2H), 0.93-0.87 (m, 6H), 0.78-0.74 (m, 3H). δ ^{13}C NMR ($CDCl_3$) 176.51, 139.84, 128.54, 128.15, 126.17, 126.15, 72.50, 68.92, 47.66, 44.52, 44.49, 38.49, 32.05, 29.38, 29.35, 23.90, 22.24, 21.20, 16.02.

Example 2 (General Procedure)

In a flask flushed with nitrogen were placed magnesium turnings (1.05 equiv.). Little 1,2-dibromoethane and chlorotrimethylsilane were added followed by the addition of the corresponding 2-chloro-1-isopropyl-4-methylcyclohexane (1.0 equiv.) in THF (0.5 M). The reaction mixture was stirred at 70 °C for 3 h before CO_2 was added and then stirred again at 70 °C for 1 h. NMP (0.5 M) was added and the reaction mixture was stirred at 80 °C for 1 h. After the addition of 2-bromo-1-phenylethanone (1.0 equiv.) in NMP (1.0 M), the reaction mixture was stirred at 80 °C overnight, cooled to 25 °C and poured on 2 M aqueous HCl-solution. The aqueous layer was extracted with MTBE (2 x), the combined organic phases were washed with 50% saturated aqueous $NaHCO_3$-solution, dried ($MgSO_4$), filtered and the filtrate was concentrated. The residue was purified by flash chromatography on SiO_2 and HPLC.

Example 2a



(1R,2S,5R)-2-oxo-2-phenylethyl 2-isopropyl-5-methylcyclohexanecarboxylate, (1S,2S,5R)-2-oxo-2-phenylethyl 2-isopropyl-5-methylcyclohexanecarboxylate and 2-((1R,2S,5R)-2-isopropyl-5-methylcyclohexyl)-2-oxoethyl benzoate: According to the General Procedure, starting from Mg (2.55 g, 105 mmol, 1.05 equiv.), (1S,2R,4R)-2-chloro-1-isopropyl-4-methylcyclohexane (17.5 g, 100 mmol, 1.0 equiv.) and 2-bromo-1-phenylethanone (19.9 g, 100 mmol, 1.0 equiv.), 13.3 g (44%) of (1R,2S,5R)-2-oxo-2-phenylethyl 2-isopropyl-5-methylcyclohexanecarboxylate, 4.57 g (15%) of (1S,2S,5R)-2-oxo-2-phenylethyl 2-isopropyl-5-methylcyclohexanecarboxylate and 0.30 g (1%) of 2-

((1R,2S,5R)-2-isopropyl-5-methylcyclohexyl)-2-oxoethyl benzoate were obtained after purification by flash chromatography on SiO_2 and HPLC.

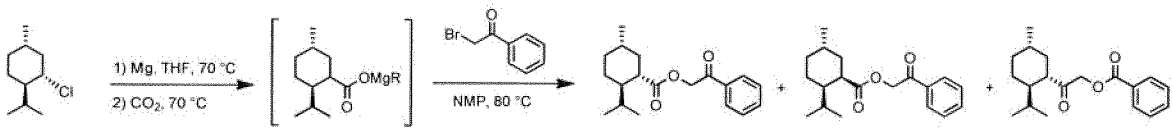
(1R,2S,5R)-2-oxo-2-phenylethyl 2-isopropyl-5-methylcyclohexanecarboxylate (**72-5396**): $[\alpha]D^{23.0}$ −35.4° (*c* 0.96, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz): 7.94-7.91 (m, 2 H), 7.63-7.59 (m, 1 H), 7.51-7.47 (m, 2 H), 5.37 (AB, J = 16.4 Hz, 1 H), 5.28 (AB, J = 16.2 Hz, 1 H), 2.50 (td, J = 11.7, 2.0 Hz, 1 H), 2.05-2.00 (m, 1 H), 1.84-1.68 (m, 3 H), 1.63-1.56 (m., 1 H), 1.46-1.38 (m, 1 H), 1.32-1.23 (m, 1 H), 1.12-0.90 (m, 8 H), 0.84 (d, J = 7.1 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz): 192.5 (C), 175.6 (C), 134.4 (C), 133.7 (CH), 128.8 (2 CH), 127.8 (2 CH), 65.6 (CH_2), 47.5 (CH), 44.3 (CH), 38.9 (CH_2), 34.5 (CH_2), 32.2 (CH), 29.1 (CH), 23.8 (CH_2), 22.3 (CH_3), 21.3 (CH_3), 16.0 (CH_3).

(1S,2S,5R)-2-oxo-2-phenylethyl 2-isopropyl-5-methylcyclohexanecarboxylate: ^1H NMR ($CDCl_3$, 400 MHz): 7.93-7.91 (m, 2 H), 7.62-7.58 (m, 1 H), 7.51-7.47 (m, 2 H), 5.34 (AB, J = 16.4 Hz, 1 H), 5.27 (AB, J = 16.2 Hz, 1 H), 3.11-3.08 (m, 1 H), 2.13-2.09 (m, 1 H), 1.82-1.64 (m, 5 H), 1.22 (ddd, J = 13.5, 12.3, 5.3 Hz, 1 H), 1.08-0.87 (m, 11 H). ^{13}C NMR ($CDCl_3$, 100 MHz): 192.7 (C), 174.1 (C), 134.5 (C), 133.7 (CH), 128.8 (2 CH), 127.8 (2 CH), 65.4 (CH_2), 46.6 (CH), 41.8 (CH), 38.1 (CH_2), 35.3 (CH_2), 30.3 (CH), 27.5 (CH), 25.7 (CH_2), 22.4 (CH_3), 21.6 (CH_3), 21.2 (CH_3).

2-((1R,2S,5R)-2-isopropyl-5-methylcyclohexyl)-2-oxoethyl benzoate: ^1H NMR ($CDCl_3$, 400 MHz): 8.12-8.10 (m, 2 H), 7.61-7.57 (m, 1 H), 7.49-7.44 (m, 2 H), 5.01 (AB, J = 16.9 Hz, 1 H), 4.88 (AB, J = 16.9 Hz, 1 H), 2.62-2.56 (m, 1 H), 1.91-1.85 (m, 1 H), 1.79-1.65 (m, 4 H), 1.45-1.35 (m, 1 H), 1.15-0.91 (m, 9 H), 0.83 (d, J = 6.8 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz): 207.1 (C), 165.9 (C), 133.3 (CH), 129.9 (2 CH), 129.4 (C), 128.4 (2 CH), 68.1 (CH_2), 50.5 (CH), 43.8 (CH), 38.7

(CH_2), 34.4 (CH_2), 32.5 (CH), 28.8 (CH), 23.8 (CH_2), 22.3 (CH_3), 21.4 (CH_3), 16.1 (CH_3).

Example 2b



(1S,2R,5S)-2-oxo-2-phenylethyl 2-isopropyl-5-methylcyclohexanecarboxylate, (1R,2R,5S)-2-oxo-2-phenylethyl 2-isopropyl-5-methylcyclohexanecarboxylate and 2-((1S,2R,5S)-2-isopropyl-5-methylcyclohexyl)-2-oxoethyl benzoate: According to the General Procedure, starting from Mg (293 mg, 12.1 mmol, 1.05 equiv.), (1R,2S,4S)-2-chloro-1-isopropyl-4-methylcyclohexane (2.19 g, 11.5 mmol, 1.0 equiv.) and 2-bromo-1-phenylethanone (2.29 g, 11.5 mmol, 1.0 equiv.), 2.36 g (68%) of (1S,2R,5S)-2-oxo-2-phenylethyl 2-isopropyl-5-methylcyclohexanecarboxylate, 0.56 g (16%) of (1R,2R,5S)-2-oxo-2-phenylethyl 2-isopropyl-5-methylcyclohexanecarboxylate and 0.11 g (3%) of 2-((1S,2R,5S)-2-isopropyl-5-methylcyclohexyl)-2-oxoethyl benzoate were obtained after purification by flash chromatography on SiO_2 and HPLC.

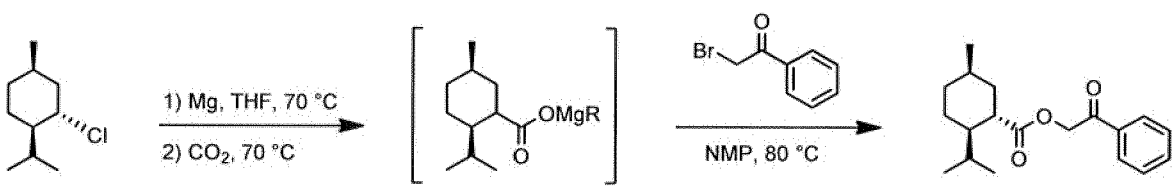
(1S,2R,5S)-2-oxo-2-phenylethyl 2-isopropyl-5-methylcyclohexanecarboxylate: $[\alpha]D^{23.0}$ +34.5° (*c* 0.99, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz): 7.94-7.91 (m, 2 H), 7.63-7.59 (m, 1 H), 7.51-7.47 (m, 2 H), 5.37 (AB, J = 16.4 Hz, 1 H), 5.28 (AB, J = 16.4 Hz, 1 H), 2.50 (td, J = 11.6, 3.5 Hz, 1 H), 2.05-2.00 (m, 1 H), 1.84-1.68 (m, 3 H), 1.62-1.56 (m., 1 H), 1.45-1.39 (m, 1 H), 1.32-1.23 (m, 1 H), 1.12-0.90 (m, 8 H), 0.84 (d, J = 7.1 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz): 192.5 (C), 175.6 (C), 134.4 (C), 133.7 (CH), 128.8 (2 CH), 127.8 (2 CH), 65.6 (CH_2), 47.5 (CH), 44.3 (CH),

38.9 (CH_2), 34.5 (CH_2), 32.2 (CH), 29.1 (CH), 23.8 (CH_2), 22.3 (CH_3), 21.3 (CH_3), 16.0 (CH_3).

(1R,2R,5S)-2-oxo-2-phenylethyl 2-isopropyl-5-methylcyclohexanecarboxylate: ^1H NMR ($CDCl_3$, 400 MHz): 7.94-7.91 (m, 2 H), 7.63-7.58 (m, 1 H), 7.51-7.46 (m, 2 H), 5.34 (AB, J = 16.2 Hz, 1 H), 5.27 (AB, J = 16.4 Hz, 1 H), 3.11-3.08 (m, 1 H), 2.14-2.08 (m, 1 H), 1.82-1.64 (m, 5 H), 1.22 (ddd, J = 13.6, 12.4, 5.3 Hz, 1 H), 1.08-1.00 (m, 1 H), 0.97-0.87 (m, 10 H). ^{13}C NMR ($CDCl_3$, 100 MHz): 192.7 (C), 174.1 (C), 134.5 (C), 133.7 (CH), 128.8 (2 CH), 127.8 (2 CH), 65.4 (CH_2), 46.6 (CH), 41.8 (CH), 38.1 (CH_2), 35.3 (CH_2), 30.2 (CH), 27.5 (CH), 25.7 (CH_2), 22.4 (CH_3), 21.6 (CH_3), 21.2 (CH_3).

2-((1S,2R,5S)-2-isopropyl-5-methylcyclohexyl)-2-oxoethyl benzoate: ^1H NMR ($CDCl_3$, 400 MHz): 8.12-8.10 (m, 2 H), 7.62-7.57 (m, 1 H), 7.49-7.45 (m, 2 H), 5.01 (AB, J = 16.9 Hz, 1 H), 4.89 (AB, J = 16.9 Hz, 1 H), 2.62-2.56 (m, 1 H), 1.91-1.85 (m, 1 H), 1.79-1.65 (m, 4 H), 1.45-1.35 (m, 1 H), 1.15-0.91 (m, 9 H), 0.83 (d, J = 6.8 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz): 207.1 (C), 165.9 (C), 133.3 (CH), 129.9 (2 CH), 129.4 (C), 128.4 (2 CH), 68.1 (CH_2), 50.5 (CH), 43.8 (CH), 38.7 (CH_2), 34.4 (CH_2), 32.5 (CH), 28.8 (CH), 23.8 (CH_2), 22.3 (CH_3), 21.4 (CH_3), 16.1 (CH_3).

Example 2c



(1S,2R,5R)-2-oxo-2-phenylethyl 2-isopropyl-5-methylcyclohexanecarboxylate: According to the General Procedure, starting from Mg (507 mg, 20.9 mmol, 1.05 equiv.), (1R,2S,4R)-2-chloro-1-isopropyl-4-methylcyclohexane (4.63 g, 75% Wt, 19.9 mmol, 1.0 equiv.) and 2-bromo-1-phenylethanone (3.96 g, 19.9 mmol, 1.0 equiv.), 3.70 g (62%) of 2-oxo-2-phenylethyl 2-isopropyl-5-methylcyclohexanecarboxylateas was obtained as a mixture of isomers. (1S,2R,5R)-2-oxo-2-phenylethyl 2-isopropyl-5-methylcyclohexanecarboxylate could be isolated as a single isomer after purification by flash chromatography on SiO_2 and HPLC. ^1H NMR ($CDCl_3$, 400 MHz): 7.92-7.89 (m, 2 H), 7.61-7.56 (m, 1 H), 7.49-7.45 (m, 2 H), 5.33-5.29 (m, 2 H), 2.77-2.72 (td, J = 9.1, 4.0 Hz, 1 H), 2.01-1.12 (m, 9 H), 0.97-0.86 (m, 9 H). ^{13}C NMR ($CDCl_3$, 100 MHz): 192.5 (C), 175.8 (C), 134.4 (C), 133.6 (CH), 128.7 (2 CH), 127.7 (2 CH), 65.6 (CH_2), 43.7 (CH), 41.8 (CH), 34.6 (CH_2), 30.5 (CH_2), 28.4 (CH), 27.3 (CH), 21.1 (CH_3), 19.6 (CH_2), 19.0 (CH_3), 17.4 (CH_3).

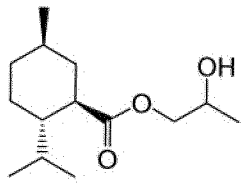
Example 3

Application in toothpaste

0.10 g of a 10% solution in ethanol of a compound of formula (I) was mixed with an opaque toothgel base to a concentration of 200ppm.

A piece (0.5 g) of the thus prepared toothpaste was weighed on a toothbrush and a panelist's teeth were brushed for 2min. The mouth was rinsed with water and the water expectorated. Panelists recorded the perceived long lasting cooling sensation over all areas of the mouth at regular time periods.

Similar opaque toothgel formulations were prepared with 800ppm WS3 and 250ppm of the comparative compound of the following formula



The cooling intensity was plotted versus time and the results are shown in the Figure.

In the Figure,

-♦- is a plot of the compound of formula (I),

-■- is a plot of the comparative compound, and

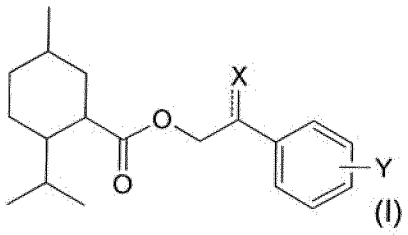
-▲- is a plot of WS3.

It is clear from the Figure 1 that improved long lasting cooling intensity is achieved with a compound of formula (I).

These examples are for the purpose of illustration only and it is understood that variations and modifications can be made by one skilled in the art without departing from the scope of the claims. It should be understood that the aspects and embodiments described above are not only in the alternative, but can also be combined.

Claims:

1. A compound of the formula (I)

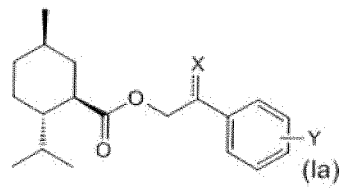


(I)

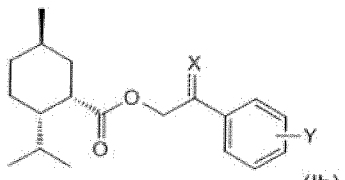
wherein

the symbol ------ represents a double bond when X is an oxygen atom or a single bond when X is a hydroxyl group, and Y represents a hydrogen atom or a substituent in the meta or para position, said substituent if present being hydroxyl, CN or $-CH_2CN$.

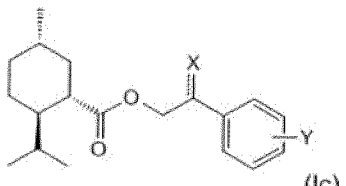
2. A compound according to claim 1 selected from



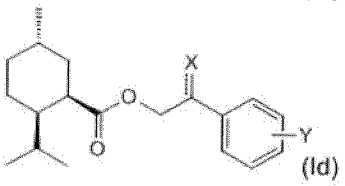
(Ia)



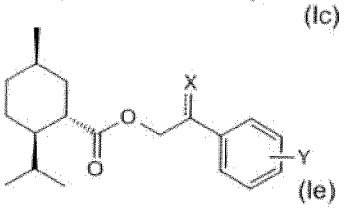
(Ib)



(Ic)



(Id) or



(Ie) .

3. A compound according to claim 2 of the formula (Ia).

4. A compound according to claim 3 wherein the symbol ------ represents a single bond and X is an hydroxyl group.

5. A consumer product composition comprising a compound according to any one of the claims 1 to 4.

6. A consumer product composition according to claim 5 wherein the compound of formula (I) is present in amounts of 3 ppm to 10000 ppm weight, based on the weight of consumer product composition into which it is incorporated.

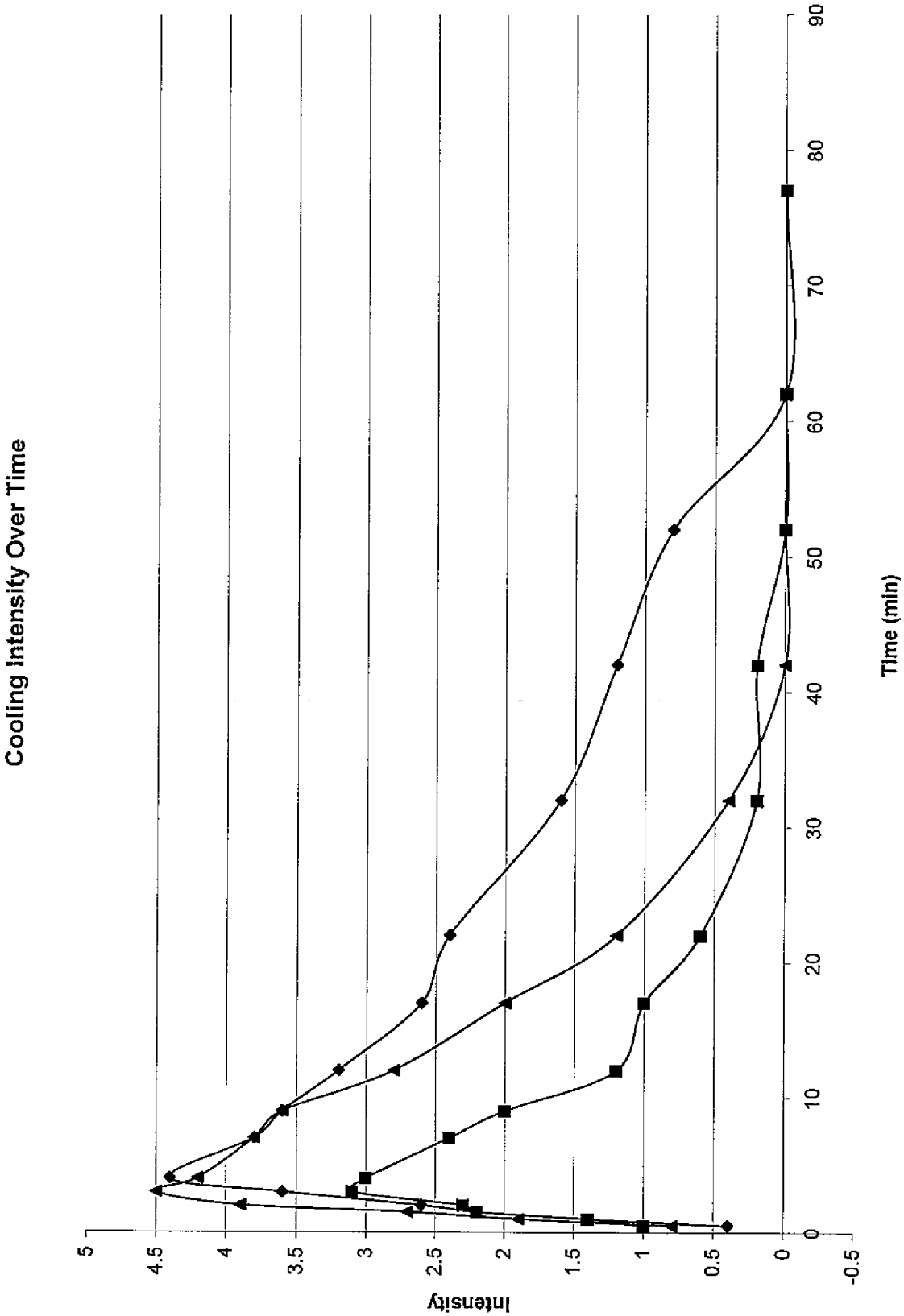
7. A method to confer, enhance, improve or modify the coolant properties of a consumer product composition, which method comprises adding to said composition a compound defined in any one of the claims 1 to 4.

8. A consumer product according to claim 5, which is an oral care product.

9. An oral care product according to claim 8 selected from the group consisting of tooth pastes, tooth gels, tooth powders, tooth whitening products, mouthwashes, lozenges, dental floss, tooth picks, anti-plaque and anti-gingivitis compositions, throat lozenges, throat drops, inflammatory compositions, compositions for treatment of nasal symptoms, cold symptoms and upper gastrointestinal tract distress, compositions for cold relief, for alleviating discomfort of hot flash, gargle compositions, breath-freshening sprays, tooth polishes, denture adhesives and mouth rinses.

10. A consumer product according to any one of the claims 5, 6 or 8 in the form of a gum.

Figure 1


Cooling Intensity Over Time
Intensity
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
-0.5
Time (min)
0
10
20
30
40
50
60
70
80
90

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2013/064494

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07C69/75
ADD.

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)
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 practicable, search terms used)
EPO-Internal, CHEM ABS Data, WPI Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 033 994 A (WATSON HUGH R ET AL) 5 July 1977 (1977-07-05) cited in the application See the examples	1-10
A	WO 2008/075942 A1 (QUEST INT SERV BV [NL]; GIVAUDAN SA [CH]; FURRER STEFFAN [US]; TONDEUR) 26 June 2008 (2008-06-26) the whole document	1-10

☐ 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

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"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

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 September 2013	26/09/2013

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Menchaca, Roberto

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2013/064494

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		JP 2010513657 A	30-04-2010
		KR 20090113829 A	02-11-2009
		US 2010056636 A1	04-03-2010
		WO 2008075942 A1	26-06-2008