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(54) **Title:** APIGENIN GLYCOSIDES FLAVOR ENHANCERS

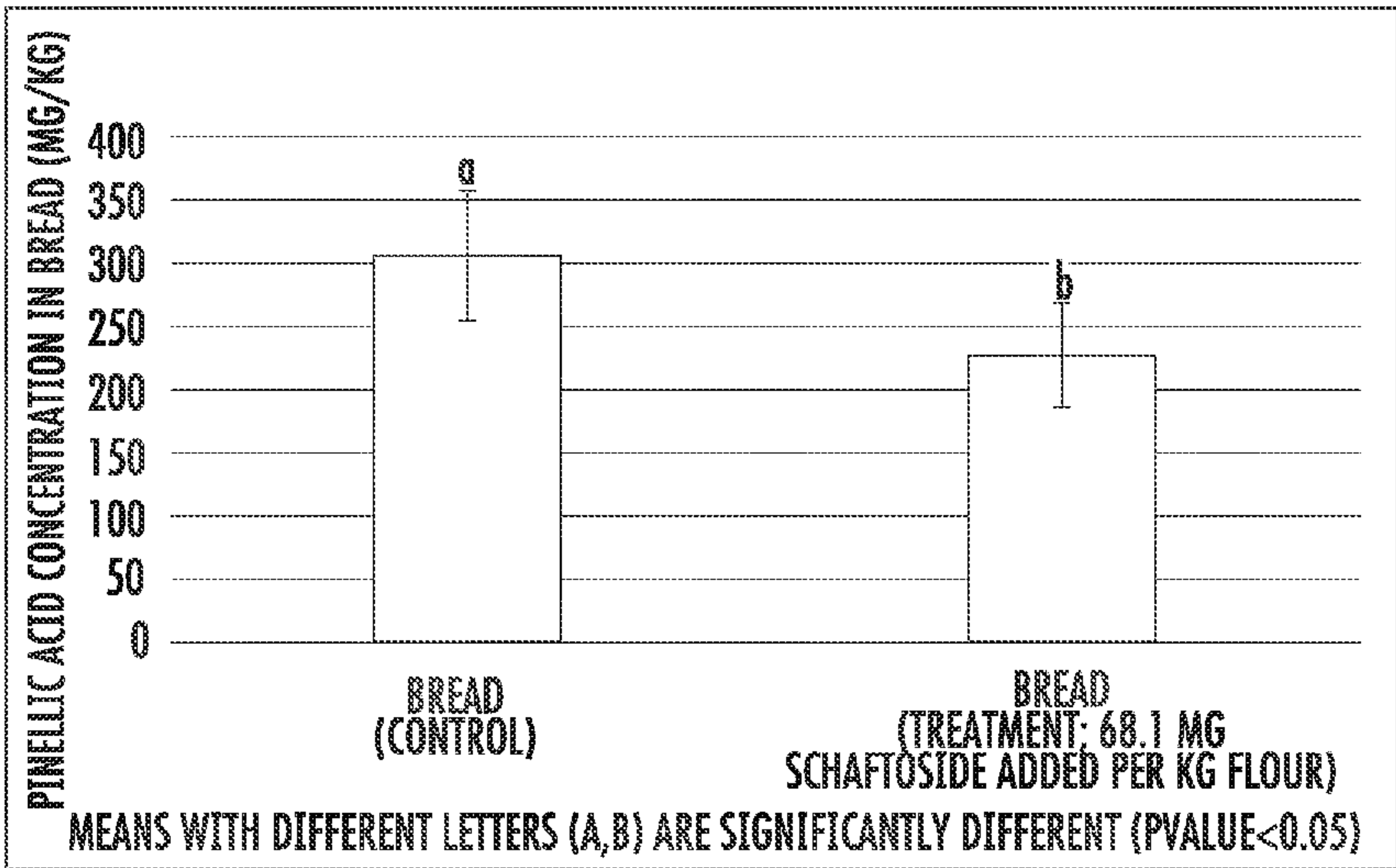


FIG. 1

(57) **Abstract:** Disclosed herein are compounds and methods useful for improving the flavor and suppressing bitter sensations is a variety of food products, including cereals and grains such as wheat.

## APIGENIN GLYCOSIDES FLAVOR ENHANCERS

### CROSS REFERENCE TO RELATED APPLICATION

This application claims the benefit of U.S. Provisional Application 62/924,896, filed on  
5 October 23, 2019, the contents of which are hereby incorporated in its entirety.

### FIELD OF THE INVENTION

The invention is directed to compounds for improving the flavor of food product,  
especially grains and cereals.

10

### BACKGROUND

Around the world, rice, wheat, maize, sorghum and millets are important staples critical  
to daily survival of billions of people. The USDA's Economic Research Service's Wheat  
Outlook report has published that global wheat production in 2019-20 is projected to reach a  
15 new record of 780.8 million tonnes (Lyddon, States, America, Commodities, & Report, 2019).  
Based on the wheat export price provided by USDA and World Bank, wheat prices were  
approximately 227 dollars per ton (Haile, Kalkuhl, & Von Braun, 2016) leading to a large  
global wheat market of \$177.24 billion. According to Statistics Market Research Consulting,  
the Global Whole Grain and High Fiber Foods market is expected to grow from \$29.4 billion  
20 in 2015 to \$46.2 billion by 2022 at a Compound Annual Growth Rate (CAGR) of 6.6%. The  
demand of whole grain and high fiber foods in Asia Pacific region is expected to grow at the  
highest rate of more than 5.5%. The main factors driving the marker growth including  
improved tastes and flavors, increasing awareness of consumer towards healthy foods as well  
as aged nutrition, childhood obesity and diabetes in the United States, etc.

25 The health benefits of whole grain intake have been linked to a reduction in chronic  
pathological conditions including heart disease, cancer, diabetes, and a reduced risk of weight  
gain leading to the USDA recommendation for at least half of all grain intake be from whole  
grain sources (*Nutr. Today* **47**, 245 (2012)). Currently across all age-sex groups, whole grain  
intake on average is far below the recommended levels. Consumers, however, are becoming  
30 increasingly aware of the contribution of whole grains to a healthy diet. This awareness, driven  
by dietary guidance, is evidenced by national surveys indicating two-thirds of consumers  
consider whole grains an important factor when making purchasing decisions (*Nutr. J.* **15**, 8  
(2016)). The limiting factor in increasing whole grain consumption has largely been related to  
production challenges hindering the development of high flavor quality products. Whole wheat

products are generally associated with several negative flavor attributes such as graininess, negative wheat-like taste, oxidized aroma notes, and an overall flavor-muting phenomenon and in particular bitterness, which is also an innate taste aversion in humans (*Cell. Mol. Life Sci.* **66**, 1661 (2009)).

5           There remains a need to improve the flavor of grain-based foods, including whole grain foods. There remains a need to reduce bitter flavors associated with grain-based foods.

## SUMMARY

10           Disclosed herein are methods of improving the flavor of food products by incorporating an flavor-modulating compound. In some instances the compound is an apigenin glycoside, for example an apigenin C-glycoside.

          The details of one or more embodiments are set forth in the descriptions below. Other features, objects, and advantages will be apparent from the description and from the claims.

## BRIEF DESCRIPTION OF THE FIGURES

15           Figure 1 depicts pinellic acid concentrations for control bread and for treatment bread where 68.1 mg Schaftoside was added per kg flour prior to bread making.

## DETAILED DESCRIPTION

20           Before the present methods and systems are disclosed and described, it is to be understood that the methods and systems are not limited to specific synthetic methods, specific components, or to particular compositions. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only and is not intended to be limiting.

25           As used in the specification and the appended claims, the singular forms “a,” “an” and “the” include plural referents unless the context clearly dictates otherwise. Ranges may be expressed herein as from “about” one particular value, and/or to “about” another particular value. When such a range is expressed, another embodiment includes— from the one particular value and/or to the other particular value. Similarly, when values are expressed as approximations, by use of the antecedent “about,” it will be understood that the particular  
30           value forms another embodiment. It will be further understood that the endpoints of each of the ranges are significant both in relation to the other endpoint, and independently of the other endpoint.

“Optional” or “optionally” means that the subsequently described event or circumstance may or may not occur, and that the description includes instances where said event or circumstance occurs and instances where it does not.

Throughout the description and claims of this specification, the word “comprise” and variations of the word, such as “comprising” and “comprises,” means “including but not limited to,” and is not intended to exclude, for example, other additives, components, integers or steps. “Exemplary” means “an example of” and is not intended to convey an indication of a preferred or ideal embodiment. “Such as” is not used in a restrictive sense, but for explanatory purposes.

Disclosed are components that can be used to perform the disclosed methods and systems. These and other components are disclosed herein, and it is understood that when combinations, subsets, interactions, groups, etc. of these components are disclosed that while specific reference of each various individual and collective combinations and permutation of these may not be explicitly disclosed, each is specifically contemplated and described herein, for all methods and systems. This applies to all aspects of this application including, but not limited to, steps in disclosed methods. Thus, if there are a variety of additional steps that can be performed it is understood that each of these additional steps can be performed with any specific embodiment or combination of embodiments of the disclosed methods.

The term “alkyl” as used herein is a branched or unbranched hydrocarbon group such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, t-butyl, pentyl, hexyl, heptyl, octyl, nonyl, decyl, dodecyl, and the like. The alkyl group can also be substituted or unsubstituted. Unless stated otherwise, the term “alkyl” contemplates both substituted and unsubstituted alkyl groups. The alkyl group can be substituted with one or more groups including, but not limited to, alkoxy, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, aldehyde, amino, carboxylic acid, ester, ether, halide, hydroxy, ketone, nitro, silyl, sulfo-oxo, or thiol. An alkyl group which contains no double or triple carbon-carbon bonds is designated a saturated alkyl group, whereas an alkyl group having one or more such bonds is designated an unsaturated alkyl group. Unsaturated alkyl groups having a double bond can be designated alkenyl groups, and unsaturated alkyl groups having a triple bond can be designated alkynyl groups. Unless specified to the contrary, the term alkyl embraces both saturated and unsaturated groups.

The term “cycloalkyl” as used herein is a non-aromatic carbon-based ring composed of at least three carbon atoms. Examples of cycloalkyl groups include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, etc. The term “heterocycloalkyl” is a cycloalkyl group as defined above where at least one of the carbon atoms of the ring is

replaced with a heteroatom such as, but not limited to, nitrogen, oxygen, sulfur, selenium or phosphorus. The cycloalkyl group and heterocycloalkyl group can be substituted or unsubstituted. Unless stated otherwise, the terms “cycloalkyl” and “heterocycloalkyl” contemplate both substituted and unsubstituted cycloalkyl and heterocycloalkyl groups. The cycloalkyl group and heterocycloalkyl group can be substituted with one or more groups including, but not limited to, alkyl, alkoxy, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, aldehyde, amino, carboxylic acid, ester, ether, halide, hydroxy, ketone, nitro, silyl, sulfo-oxo, or thiol. A cycloalkyl group which contains no double or triple carbon-carbon bonds is designated a saturated cycloalkyl group, whereas a cycloalkyl group having one or more such bonds (yet is still not aromatic) is designated an unsaturated cycloalkyl group. Unless specified to the contrary, the term cycloalkyl embraces both saturated and unsaturated, non-aromatic, ring systems.

The term “aryl” as used herein is an aromatic ring composed of carbon atoms. Examples of aryl groups include, but are not limited to, phenyl and naphthyl, etc. The term “heteroaryl” is an aryl group as defined above where at least one of the carbon atoms of the ring is replaced with a heteroatom such as, but not limited to, nitrogen, oxygen, sulfur, selenium or phosphorus. The aryl group and heteroaryl group can be substituted or unsubstituted. Unless stated otherwise, the terms “aryl” and “heteroaryl” contemplate both substituted and unsubstituted aryl and heteroaryl groups. The aryl group and heteroaryl group can be substituted with one or more groups including, but not limited to, alkyl, alkoxy, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, aldehyde, amino, carboxylic acid, ester, ether, halide, hydroxy, ketone, nitro, silyl, sulfo-oxo, or thiol.

Exemplary heteroaryl and heterocyclyl rings include: benzimidazolyl, benzofuranyl, benzothiofuranyl, benzothiophenyl, benzoxazolyl, benzoxazolynyl, benzthiazolyl, benztriazolyl, benztetrazolyl, benzisoxazolyl, benzisothiazolyl, benzimidazolynyl, carbazolyl, 4aH carbazolyl, carbolinyl, chromanyl, chromenyl, cirrnolynyl, decahydroquinolynyl, 2H,6H-1,5,2-dithiazinyl, dihydrofuro[2,3 b]tetrahydrofuran, furanyl, furazanyl, imidazolidinyl, imidazolynyl, imidazolyl, 1H-indazolyl, indolenyl, indolynyl, indolizynyl, indolyl, 3H-indolyl, isatinoyl, isobenzofuranyl, isochromanyl, isoindazolyl, isoindolynyl, isoindolyl, isoquinolynyl, isothiazolyl, isoxazolyl, methylenedioxyphenyl, morpholynyl, naphthyridinyl, octahydroisoquinolynyl, oxadiazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, oxazolidinyl, oxazolyl, oxindolyl, pyrimidinyl, phenanthridinyl, phenanthrolinyl, phenazinyl, phenothiazinyl, phenoxathinyl, phenoxazinyl, phthalazinyl, piperazinyl, piperidinyl, piperidonyl, 4-piperidonyl, piperonyl, pteridinyl, purinyl, pyranyl,

pyrazinyl, pyrazolidinyl, pyrazolinyl, pyrazolyl, pyridazinyl, pyridooxazole, pyridoimidazole, pyridothiazole, pyridinyl, pyridyl, pyrimidinyl, pyrrolidinyl, pyrrolinyl, 2H-pyrrolyl, pyrrolyl, quinazolinyl, quinolinyl, 4H-quinoliziny, quinoxalinyl, quinuclidinyl, tetrahydrofuranyl, tetrahydroisoquinolinyl, tetrahydroquinolinyl, tetrazolyl, 6H-1,2,5-thiadiazinyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, thianthrenyl, thiazolyl, thienyl, thienothiazolyl, thienooxazolyl, thienoimidazolyl, thiophenyl, and xanthenyl.

The terms “alkoxy,” “cycloalkoxy,” “heterocycloalkoxy,” “cycloalkoxy,” “aryloxy,” and “heteroaryloxy” have the aforementioned meanings for alkyl, cycloalkyl, heterocycloalkyl, aryl and heteroaryl, further providing said group is connected via an oxygen atom.

As used herein, the term “substituted” is contemplated to include all permissible substituents of organic compounds. In a broad aspect, the permissible substituents include acyclic and cyclic, branched and unbranched, carbocyclic and heterocyclic, and aromatic and nonaromatic substituents of organic compounds. Illustrative substituents include, for example, those described below. The permissible substituents can be one or more and the same or different for appropriate organic compounds. For purposes of this disclosure, the heteroatoms, such as nitrogen, can have hydrogen substituents and/or any permissible substituents of organic compounds described herein which satisfy the valencies of the heteroatoms. This disclosure is not intended to be limited in any manner by the permissible substituents of organic compounds. Also, the terms “substitution” or “substituted with” include the implicit proviso that such substitution is in accordance with permitted valence of the substituted atom and the substituent, and that the substitution results in a stable compound, *e.g.*, a compound that does not spontaneously undergo transformation such as by rearrangement, cyclization, elimination, etc. Unless specifically stated, a substituent that is said to be “substituted” is meant that the substituent can be substituted with one or more of the following: alkyl, alkoxy, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, aldehyde, amino, carboxylic acid, ester, ether, halide, hydroxy, ketone, nitro, silyl, sulfo-oxo, or thiol. In a specific example, groups that are said to be substituted are substituted with a protic group, which is a group that can be protonated or deprotonated, depending on the pH.

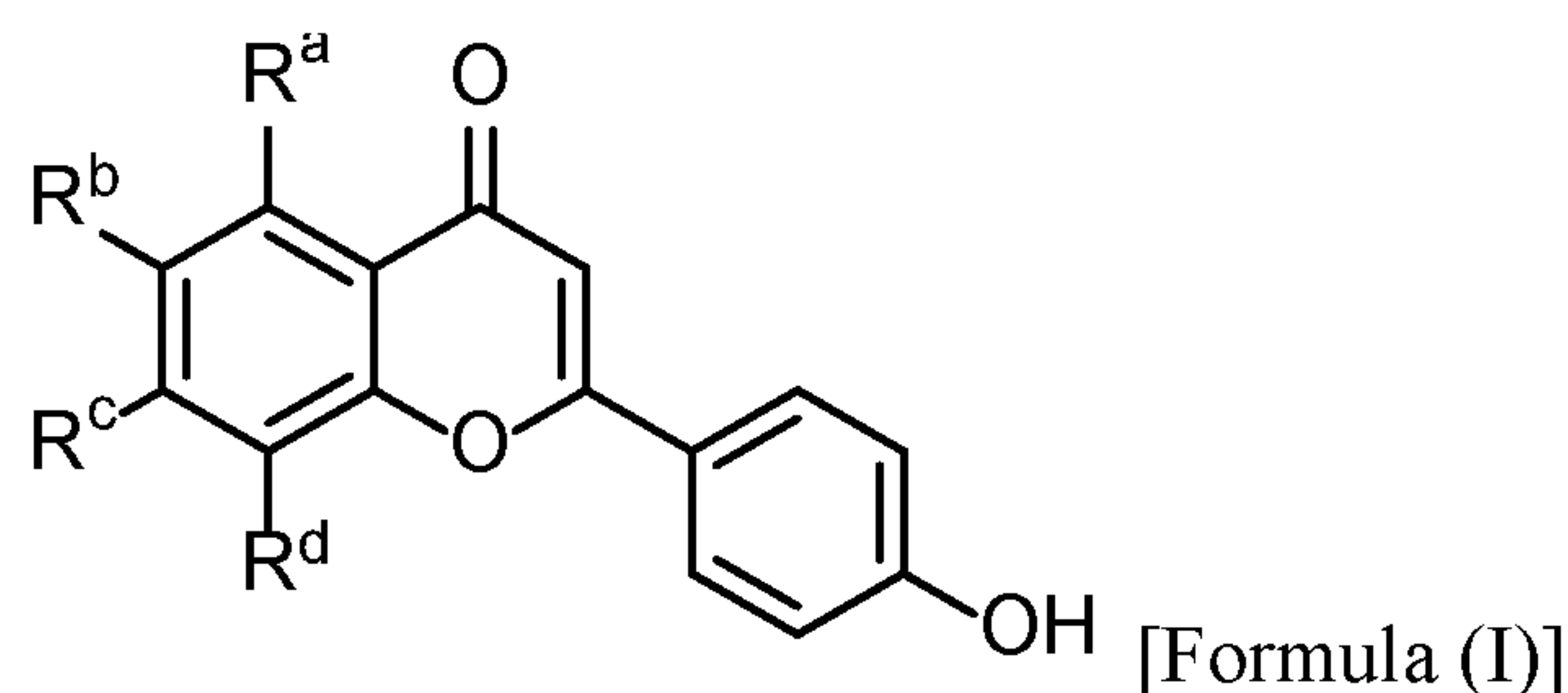
Acceptable salts are salts that retain the desired flavor modulating activity of the parent compound and do not impart undesirable toxicological effects. Examples of such salts are acid addition salts formed with inorganic acids, for example, hydrochloric, hydrobromic, sulfuric, phosphoric, and nitric acids and the like; salts formed with organic acids such as acetic, oxalic, tartaric, succinic, maleic, fumaric, gluconic, citric, malic, methanesulfonic, p-toluenesulfonic, naphthalenesulfonic, and polygalacturonic acids, and the like; salts formed from elemental

anions such as chloride, bromide, and iodide; salts formed from metal hydroxides, for example, sodium hydroxide, potassium hydroxide, calcium hydroxide, lithium hydroxide, and magnesium hydroxide; salts formed from metal carbonates, for example, sodium carbonate, potassium carbonate, calcium carbonate, and magnesium carbonate; salts formed from metal bicarbonates, for example, sodium bicarbonate and potassium bicarbonate; salts formed from metal sulfates, for example, sodium sulfate and potassium sulfate; and salts formed from metal nitrates, for example, sodium nitrate and potassium nitrate. Salts may be prepared using procedures well known in the art, for example, by reacting a sufficiently basic compound such as an amine with a suitable acid comprising a physiologically acceptable anion. Alkali metal (for example, sodium, potassium, or lithium) or alkaline earth metal (for example, calcium) salts of carboxylic acids can also be made.

Unless stated to the contrary, a formula with chemical bonds shown only as solid lines and not as wedges or dashed lines contemplates each possible isomer, e.g., each enantiomer and diastereomer, and a mixture of isomers, such as a racemic or scalemic mixture.

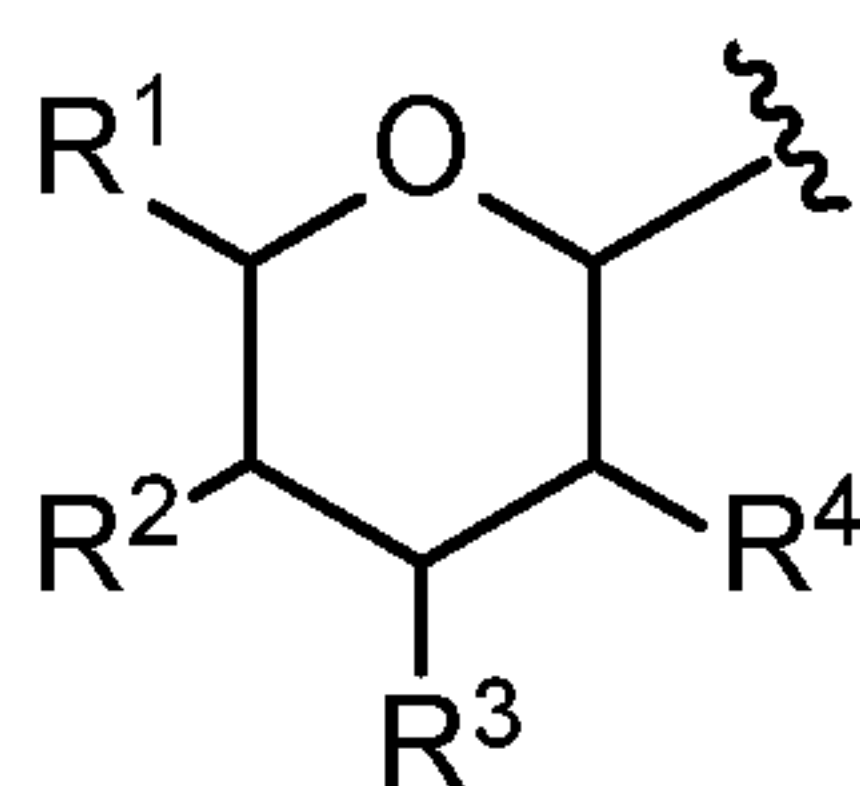
Compounds described herein can contain one or more asymmetric centers and, thus, potentially give rise to diastereomers and optical isomers. Unless stated to the contrary, the present invention includes all such possible diastereomers as well as their racemic mixtures, their substantially pure resolved enantiomers, and all possible geometric isomers.

Disclosed herein a flavor modulating apigenin O-glycosides and C-glycoside compounds. An O-glycoside refers to a carbohydrate bonded to the apigenin via an ethereal bond through the anomeric center, and a C-glycoside refers a carbohydrate directly bonded to the apigenin via a covalent bond at the anomeric, i.e., 1-position. The carbohydrates bonded to the apigenin can be hexosides and/or pentosides, and such carbohydrate can be further glycosylated with additional carbohydrate moieties. In some instances, the apigenin compound can be a compound of Formula (I):

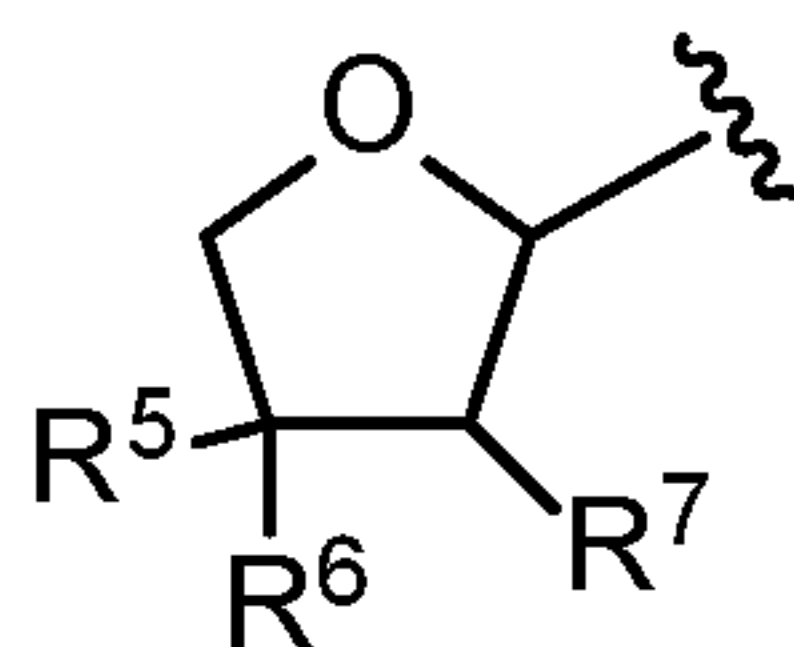


or an acceptable salt thereof, wherein  $R^a$ ,  $R^b$ ,  $R^c$ , and  $R^d$  are independently selected from H, OH, R, or OR;

wherein R is independently in each case can be a hexoside having the formula:



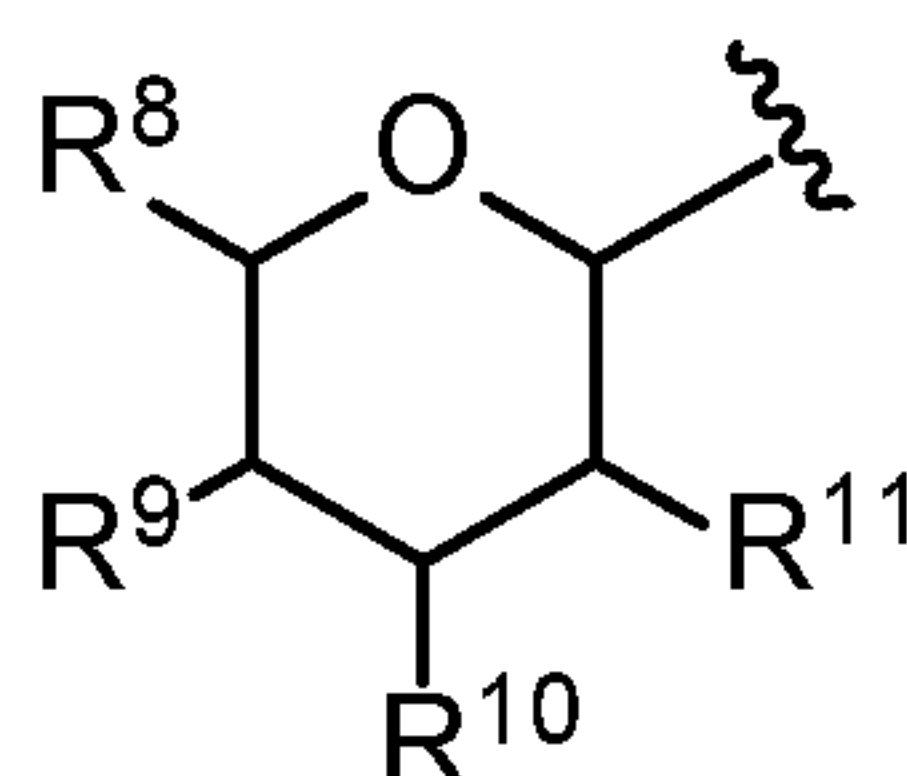
or a pentoside having the formula:



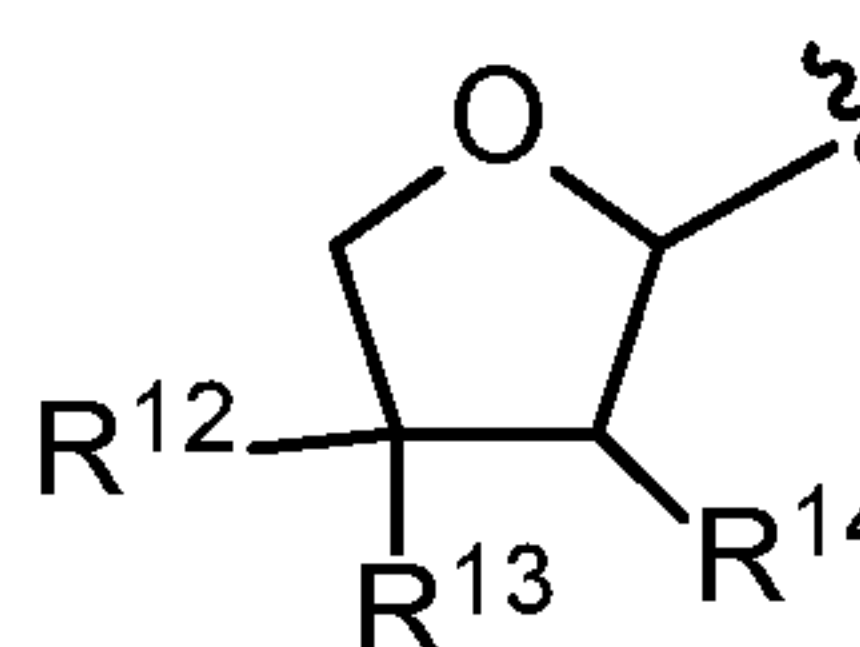
wherein R<sup>1</sup> and R<sup>5</sup> are independently selected from H, CH<sub>3</sub>, CH<sub>2</sub>OH, or CH<sub>2</sub>OR<sup>e</sup>;

5 R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>6</sup>, and R<sup>7</sup> are independently selected from H, OH, or OR<sup>e</sup>;

R<sup>e</sup> can be a hexoside having the formula:



or a pentoside having the formula:



10 wherein R<sup>8</sup> and R<sup>12</sup> are selected from H, CH<sub>3</sub> and CH<sub>2</sub>OH; and

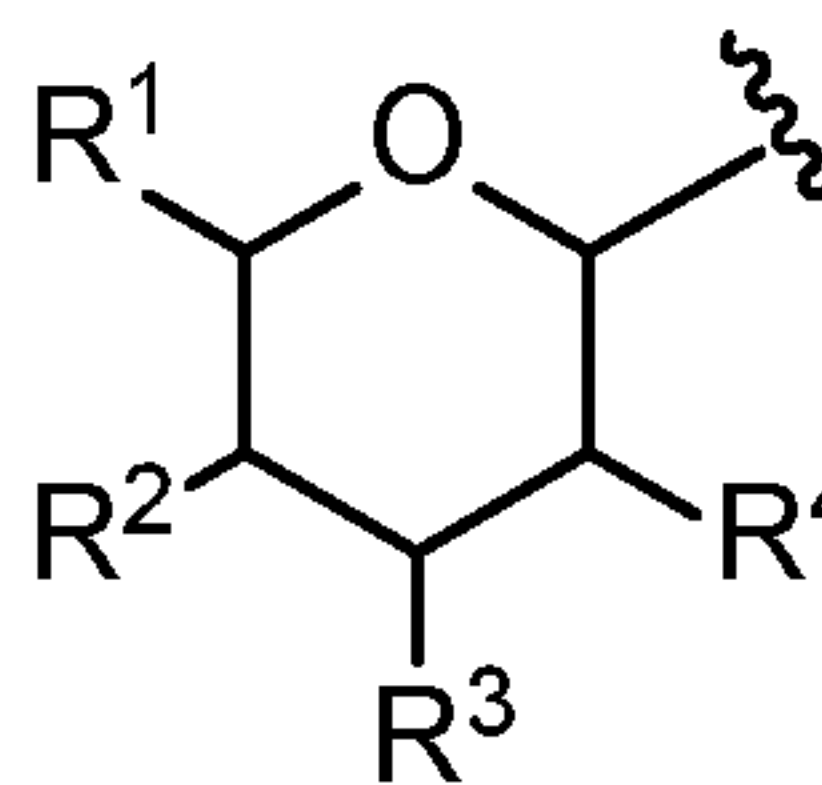
R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>13</sup>, and R<sup>14</sup> are independently selected from H and OH.

In certain embodiments, it is preferred that at least one of R<sup>a</sup>, R<sup>b</sup>, R<sup>c</sup>, and R<sup>d</sup> is R or OR, preferably a C-glycoside (i.e., R). In some embodiments, at least one R group is a hexoside.

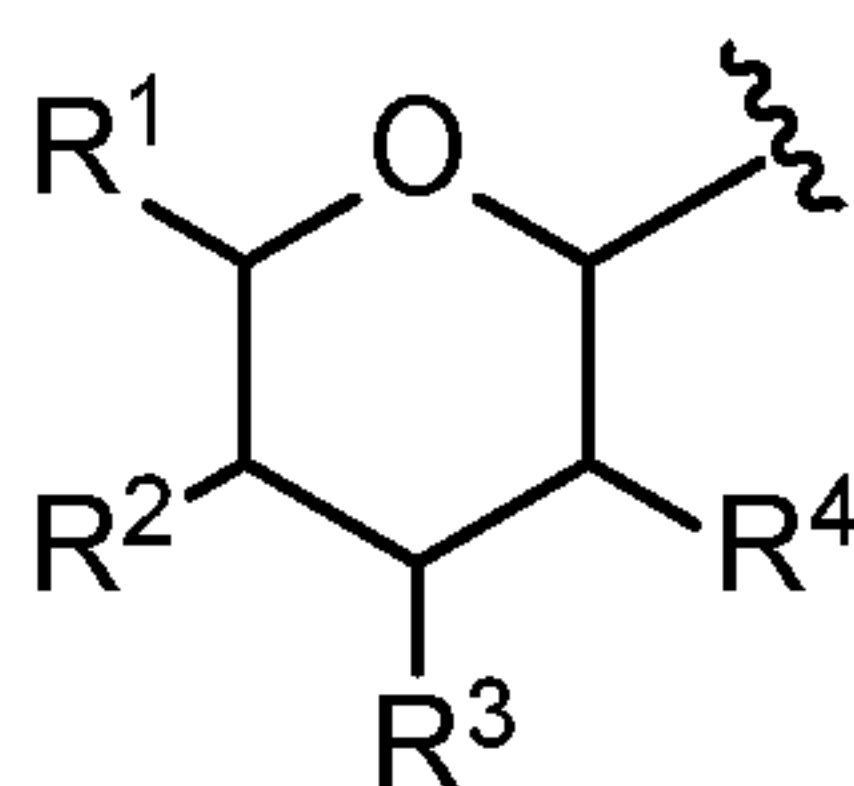
In yet further embodiments, R<sup>a</sup> and R<sup>c</sup> are each OH, and R<sup>b</sup> and R<sup>d</sup> are each R. In certain

15 embodiments, the compound of Formula (I) can be a schaftoside derivative, i.e., R<sup>a</sup> and R<sup>c</sup> are each OH;

R<sup>b</sup> is a hexoside having the formula:

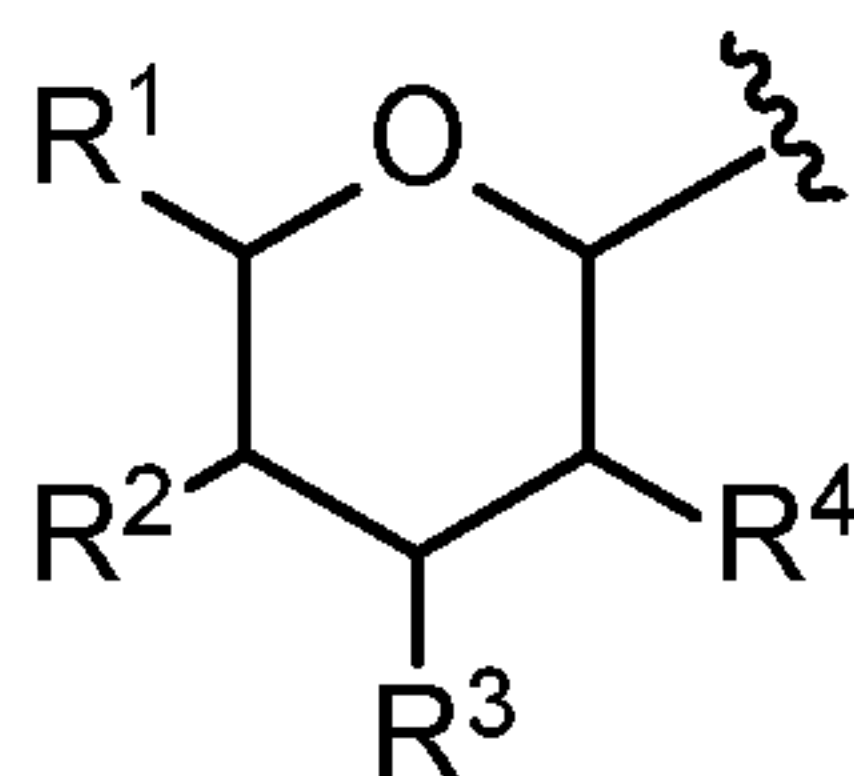


R<sup>d</sup> is a hexoside having the formula:



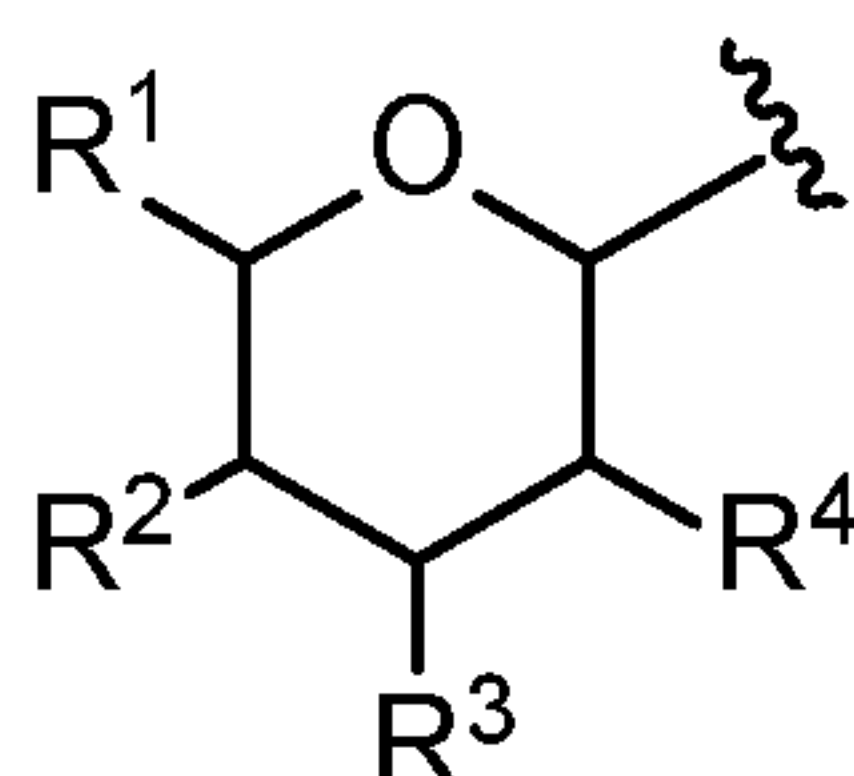
and in each instance,  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  are independently selected from the definitions given above.

In further embodiments,  $R^b$  is a hexoside having the formula:

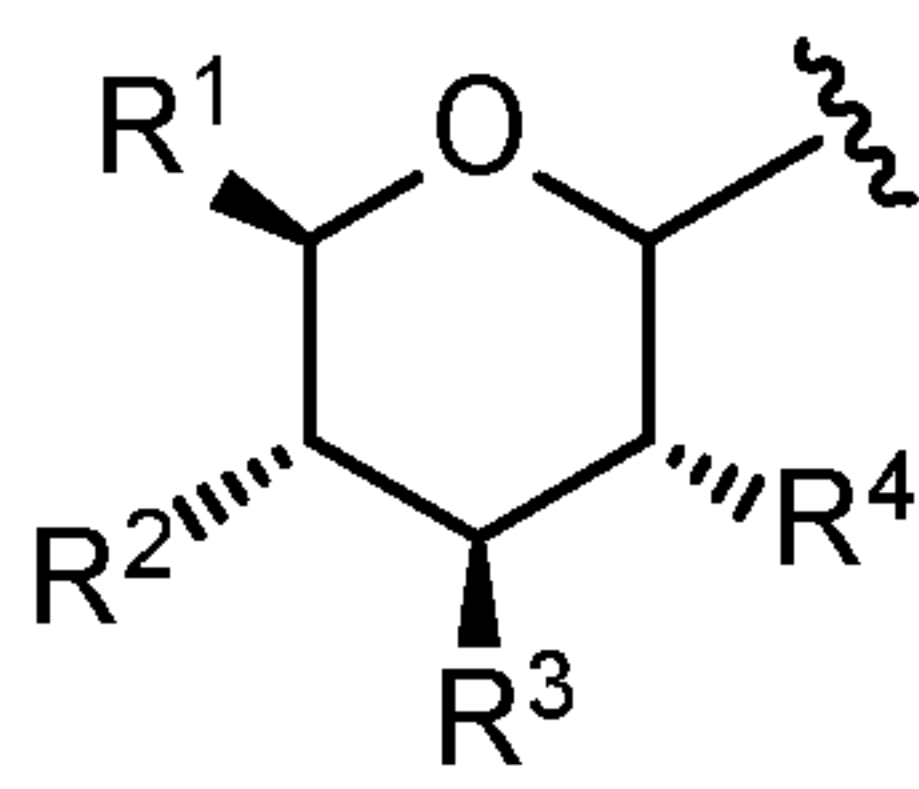


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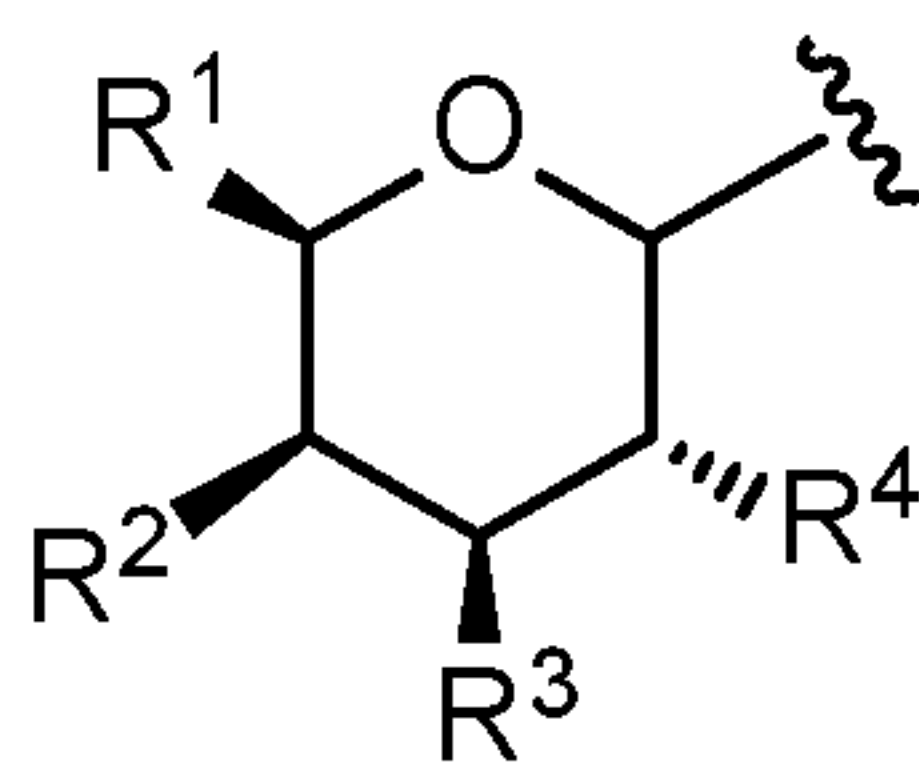
wherein  $R^1$  is  $\text{CH}_2\text{OH}$  and each of  $R^2$ ,  $R^3$ , and  $R^4$  are  $\text{OH}$ ; and  $R^d$  is a hexoside having the formula:



10 wherein  $R^1$  is  $\text{H}$  and each of  $R^2$ ,  $R^3$ , and  $R^4$  are  $\text{OH}$ . Although the stereochemistries of the pyranose rings are not particularly limited, in some embodiments  $R^b$  is a hexoside having the formula:

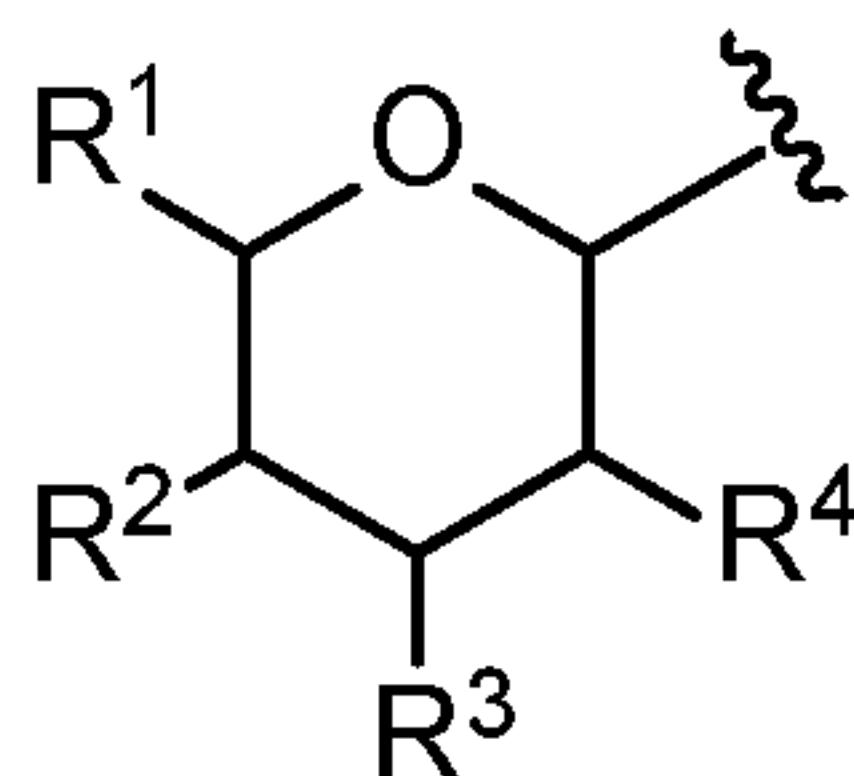


wherein  $R^1$ ,  $R^2$ ,  $R^3$  and  $R^4$  are as defined above. In yet further embodiments,  $R^d$  is a hexoside  
15 having the formula:

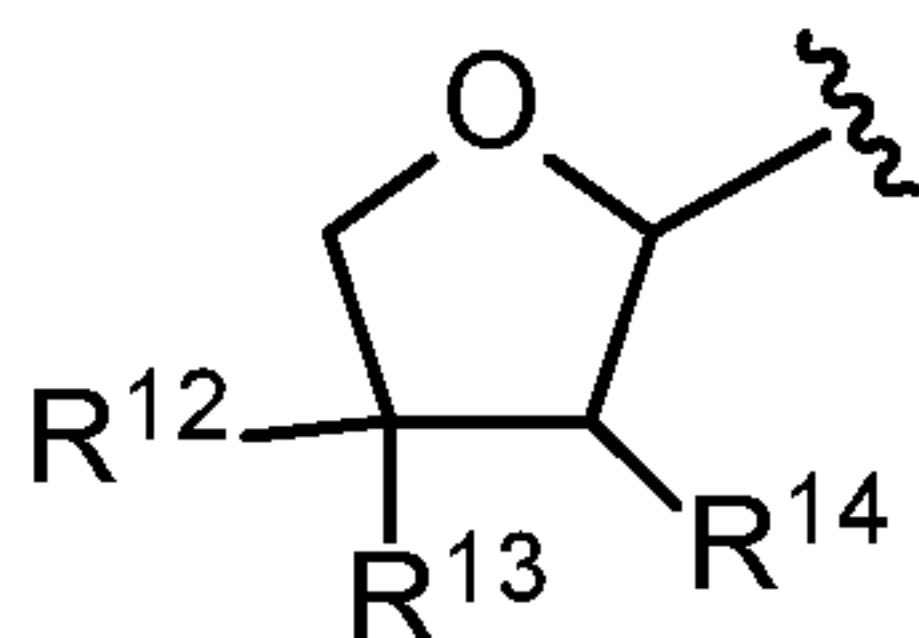


wherein  $R^1$ ,  $R^2$ ,  $R^3$  and  $R^4$  are as defined above.

In other embodiments,  $R^b$  and  $R^d$  are each hydrogen,  $R^a$  is either hydrogen or  $\text{OH}$ , and  $R^c$  is a hexoside having the formula:

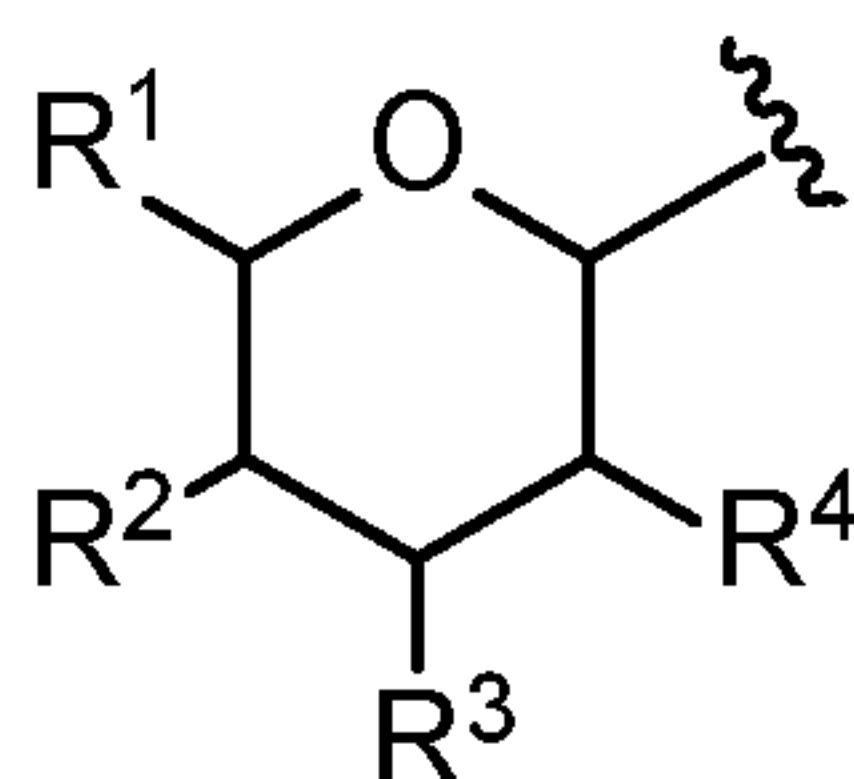


wherein  $R^1$  is  $\text{CH}_2\text{OH}$ ,  $R^2$  and  $R^3$  are each OH, and  $R^4$  is OH or  $\text{OR}^e$ , wherein  $R^e$  is a pentoside having the formula:

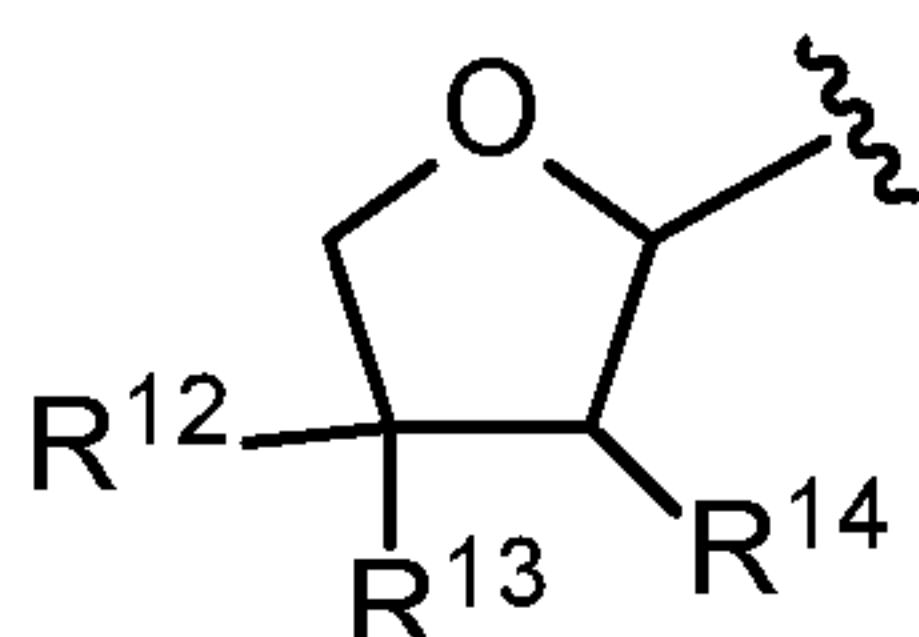


5 wherein  $R^{12}$  is  $\text{CH}_2\text{OH}$ , and  $R^{13}$  and  $R^{14}$  are each OH.

In yet further embodiments,  $R^d$  is hydrogen,  $R^a$  and  $R^c$  are independently selected from hydrogen or OH, and  $R^c$  is a hexoside having the formula:

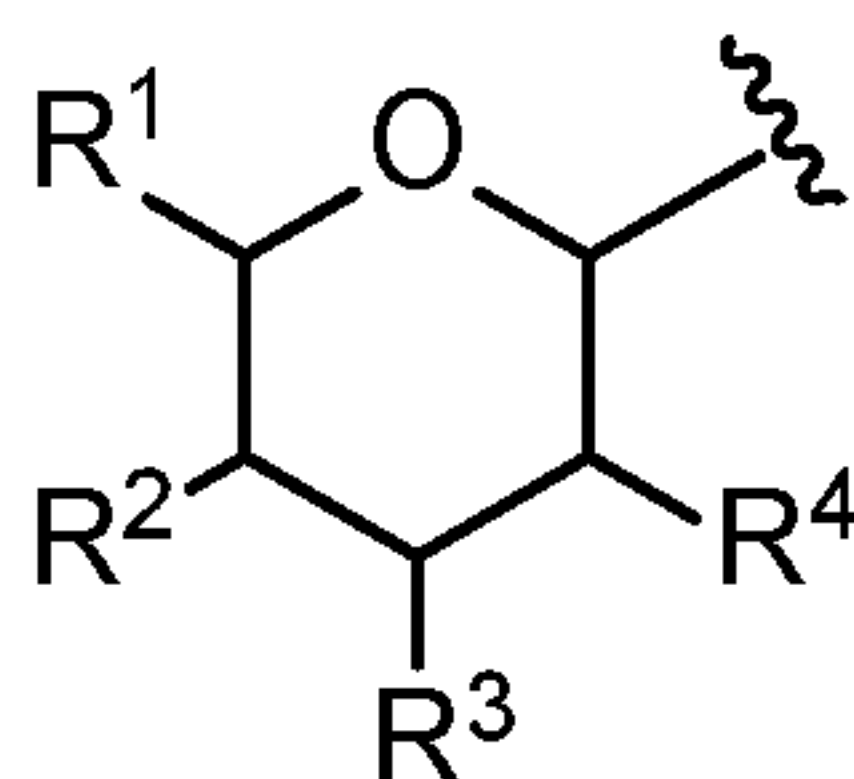


10 wherein  $R^1$  is  $\text{CH}_2\text{OH}$ ,  $R^2$  and  $R^3$  are each OH, and  $R^4$  is OH or  $\text{OR}^e$ , wherein  $R^e$  is a pentoside having the formula:

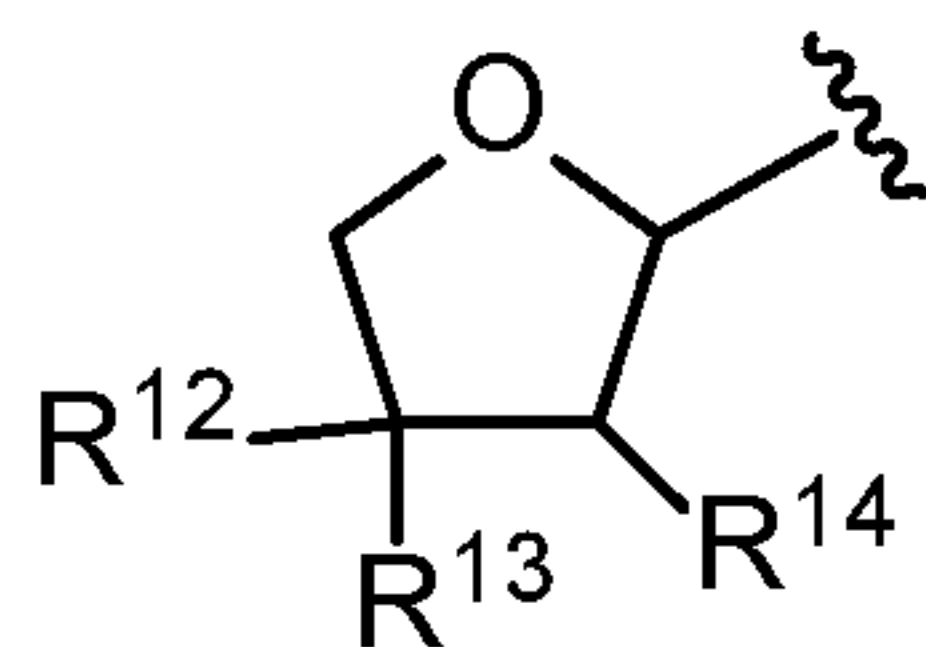


wherein  $R^{12}$  is  $\text{CH}_2\text{OH}$ , and  $R^{13}$  and  $R^{14}$  are each OH.

In yet further embodiments,  $R^a$  is hydrogen,  $R^b$  and  $R^d$  are independently selected from hydrogen or OH, and  $R^c$  is a hexoside having the formula:

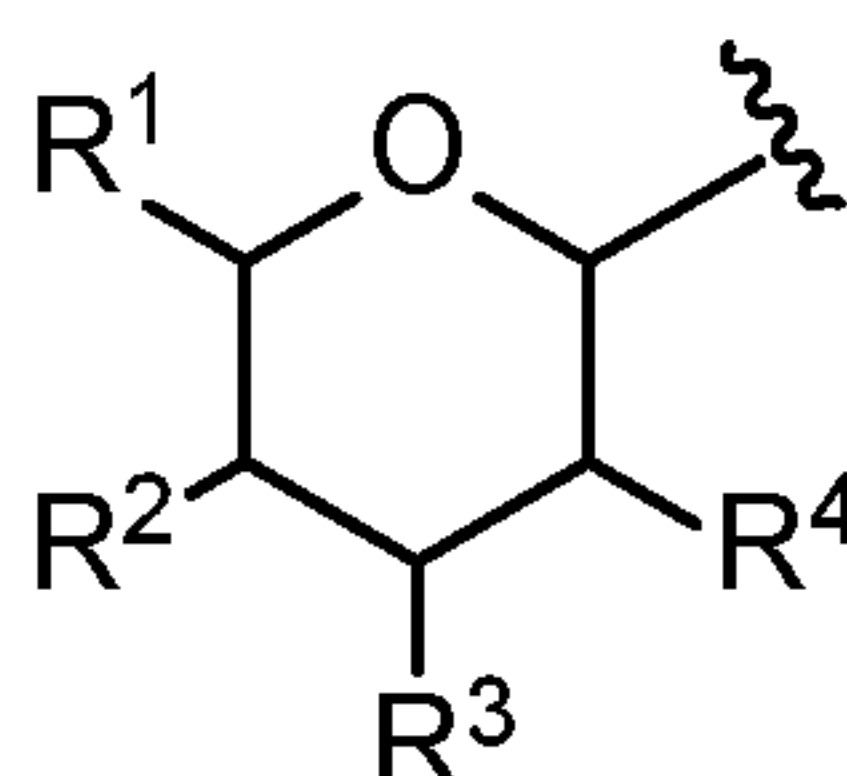


15 wherein  $R^1$  is  $\text{CH}_2\text{OH}$ ,  $R^2$  and  $R^3$  are each OH, and  $R^4$  is OH or  $\text{OR}^e$ , wherein  $R^e$  is a pentoside having the formula:



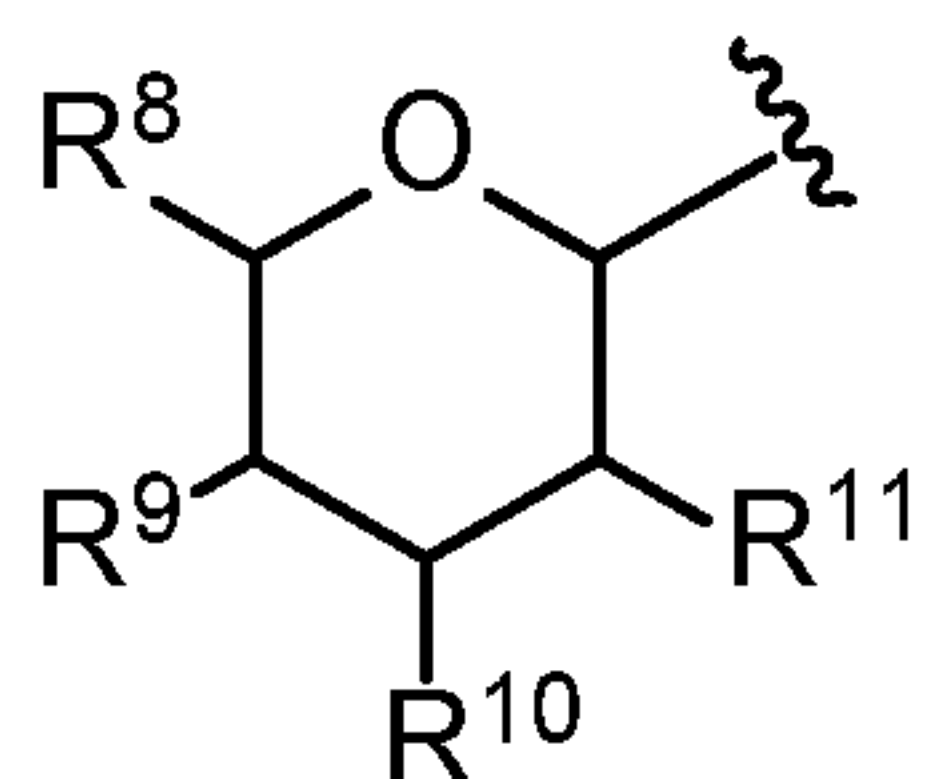
wherein R<sup>12</sup> is CH<sub>2</sub>OH, and R<sup>13</sup> and R<sup>14</sup> are each OH.

In other embodiments, R<sup>a</sup> is OH, R<sup>b</sup> and R<sup>d</sup> are independently selected from hydrogen or OH, and R<sup>c</sup> is a hexoside having the formula:



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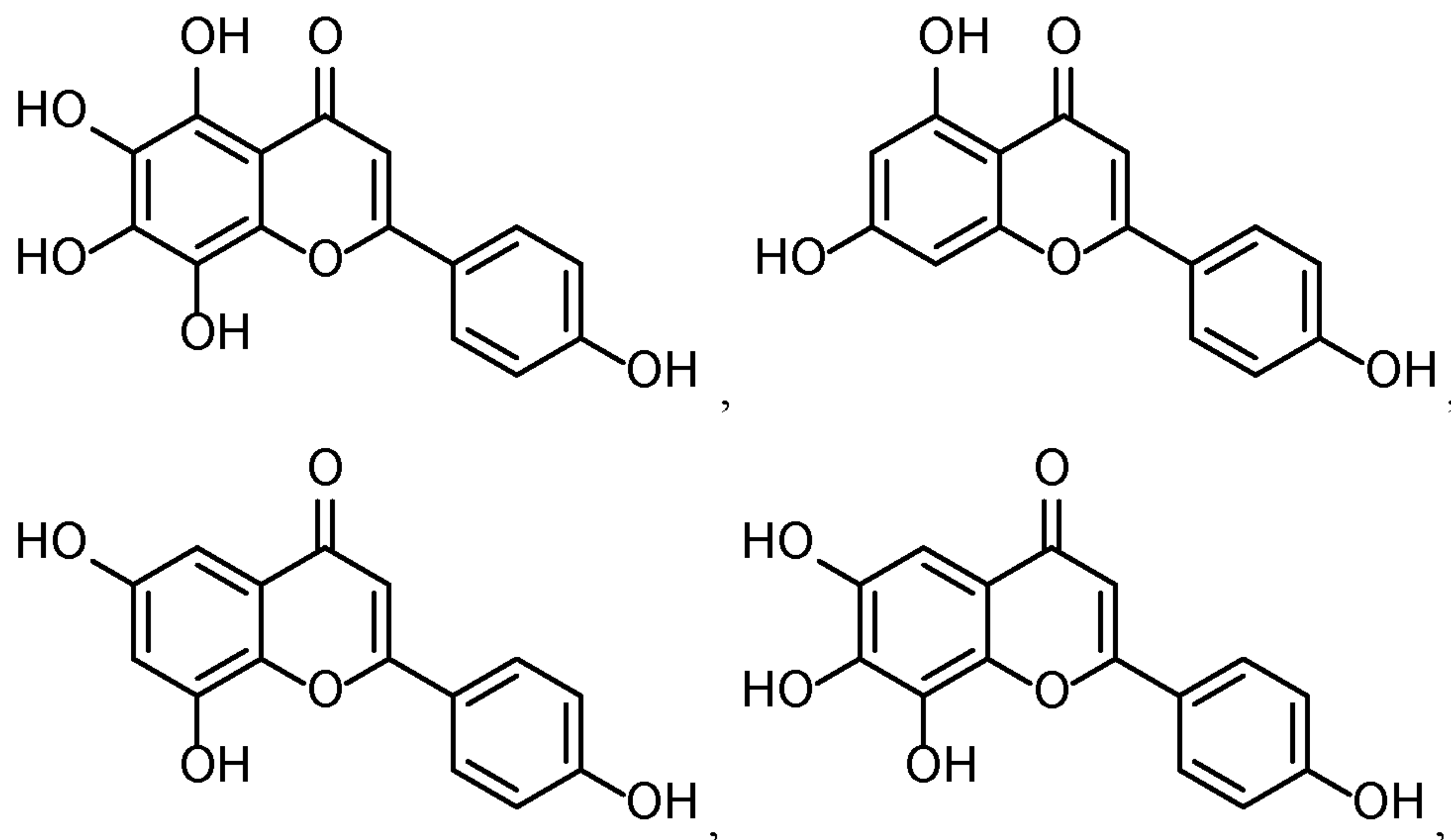
wherein R<sup>1</sup> is CH<sub>2</sub>OH, R<sup>2</sup> and R<sup>3</sup> are each OH, and R<sup>4</sup> is OH or OR<sup>e</sup>, wherein R<sup>e</sup> is a hexoside having the formula:

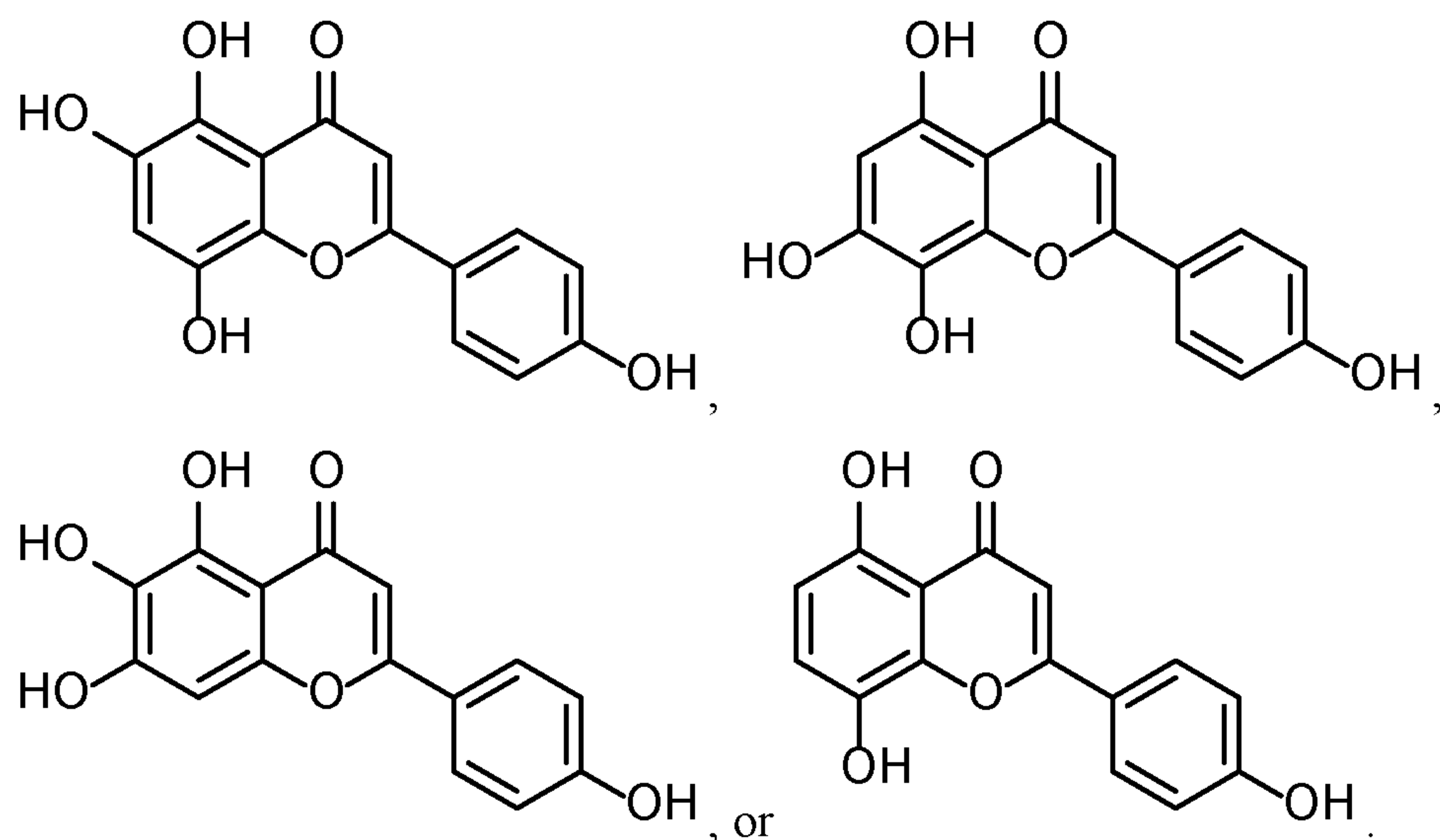


wherein R<sup>8</sup> is CH<sub>3</sub>, and R<sup>9</sup>, R<sup>13</sup>, and R<sup>14</sup> are each OH.

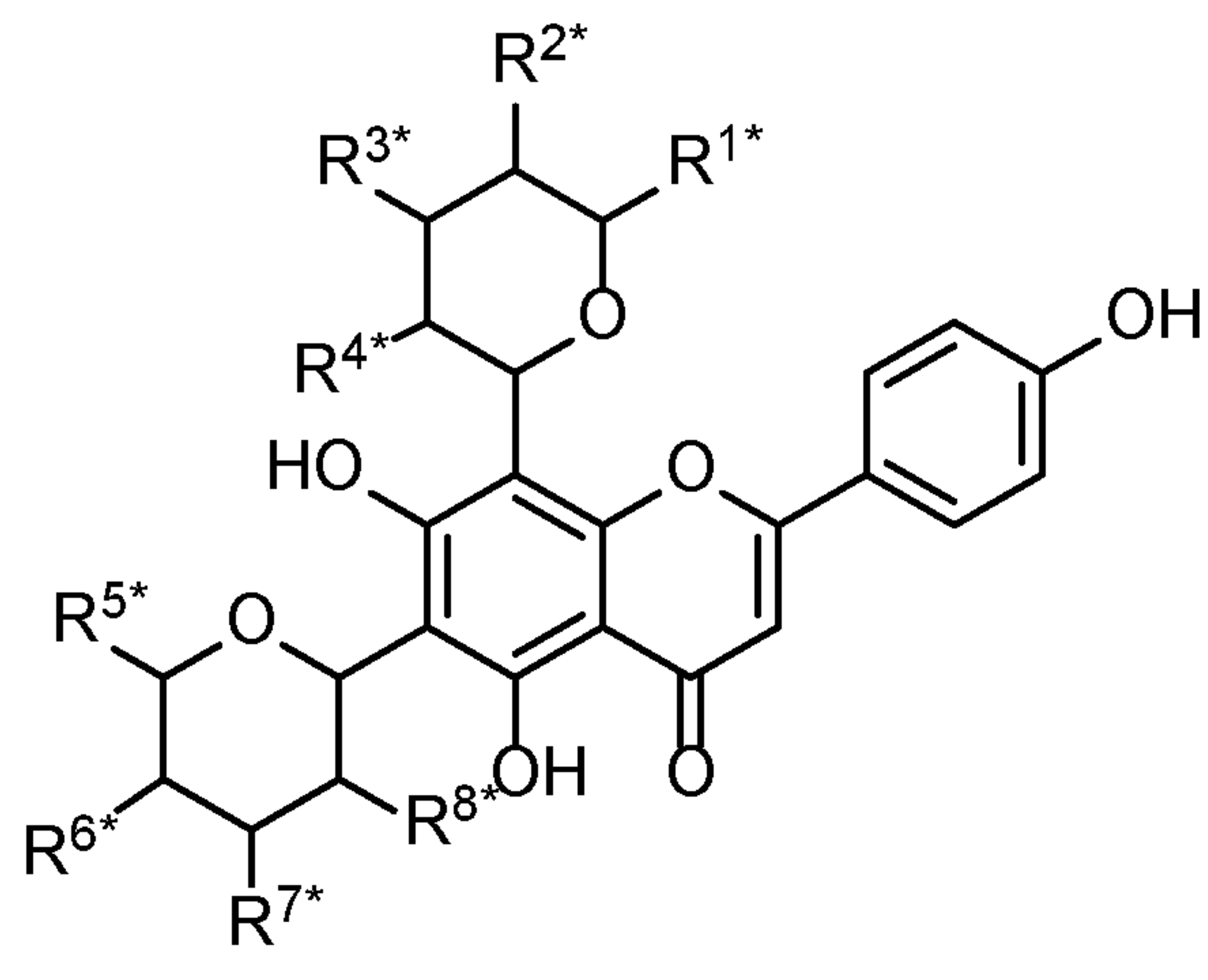
10

In certain embodiments, the flavor modulating compound is a compound having the formula:





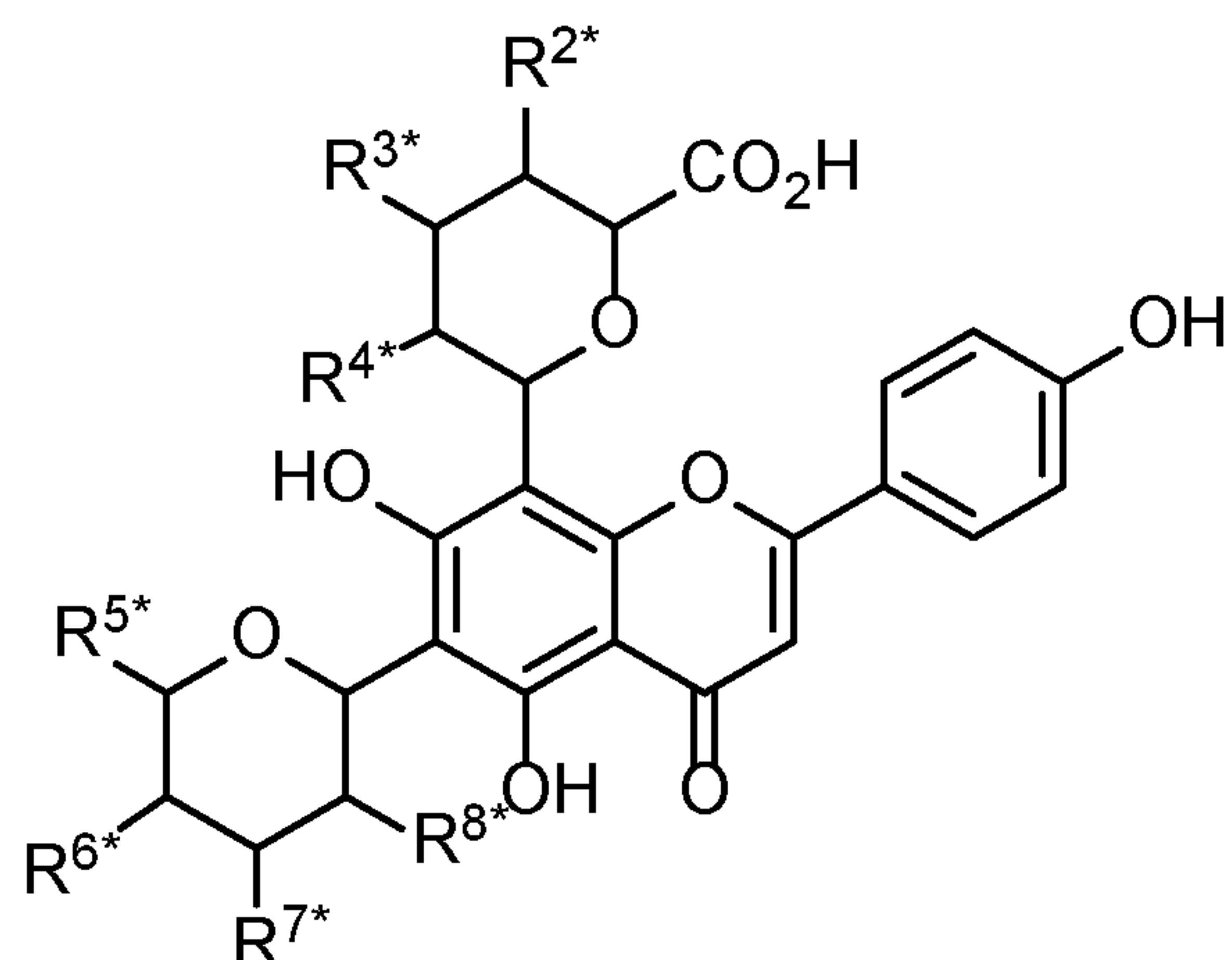
In some instances, the flavor modulating compound has the formula:



- 5 wherein R<sup>1\*</sup>, R<sup>2\*</sup>, R<sup>3\*</sup>, R<sup>4\*</sup>, R<sup>5\*</sup>, R<sup>6\*</sup>, R<sup>7\*</sup>, and R<sup>8\*</sup> are independently selected from H, (CH<sub>2</sub>)<sub>n</sub>OH, OC(O)C<sub>1-8</sub>alkyl, NHC(O)CH<sub>3</sub>, CO<sub>2</sub>H, NH<sub>2</sub>, O-C<sub>1-8</sub>alkyl, wherein n is selected from 0 or 1.

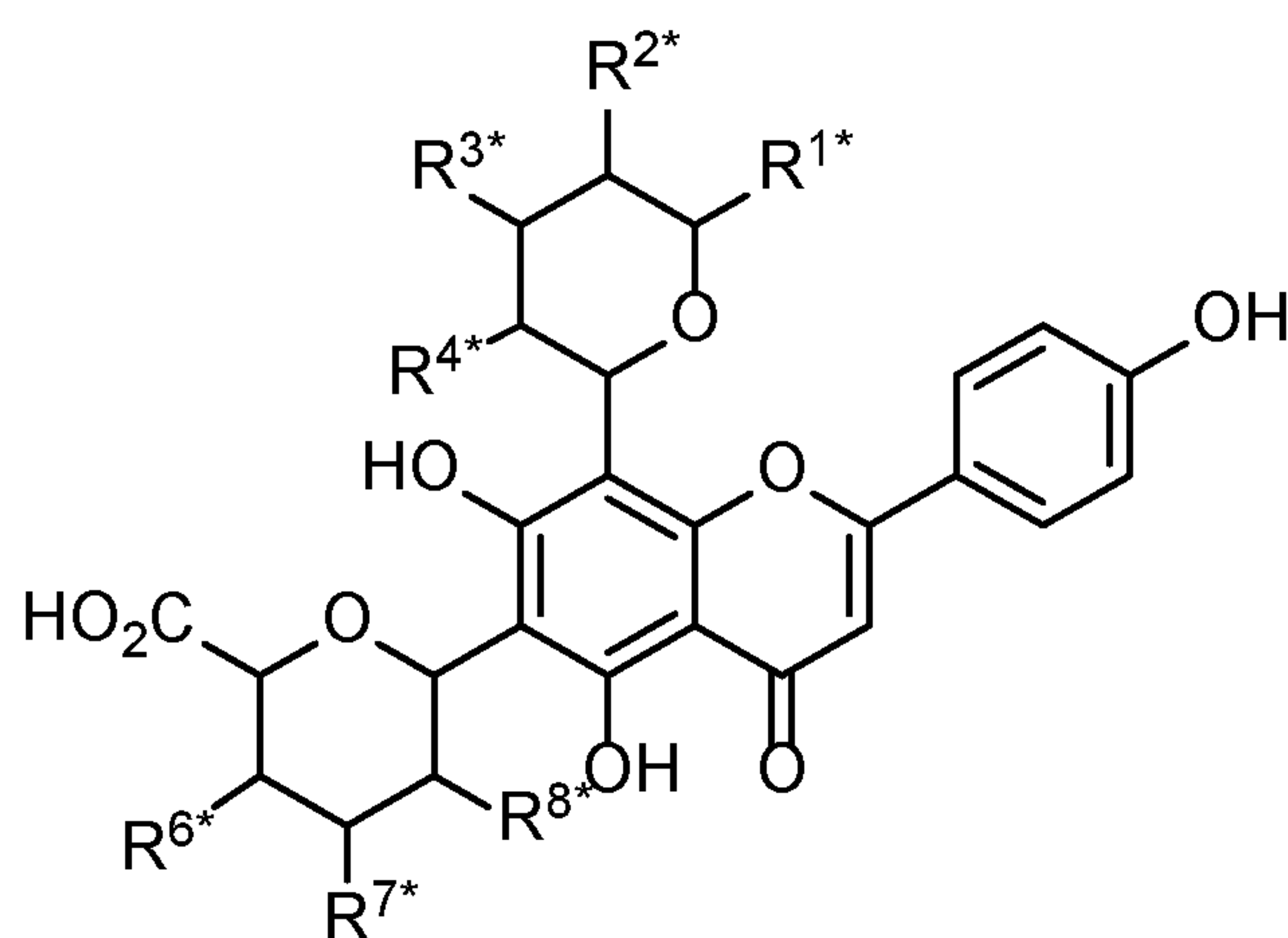
In certain embodiments, R<sup>1\*</sup> is CH<sub>2</sub>OH and R<sup>5\*</sup> is H. In further embodiments, each of R<sup>2\*</sup>, R<sup>3\*</sup>, R<sup>4\*</sup>, R<sup>6\*</sup>, R<sup>7\*</sup>, and R<sup>8\*</sup> are OH.

- 10 In some instances, the flavor modulating compound has the formula:



wherein  $R^{2*}$ ,  $R^{3*}$ ,  $R^{4*}$ ,  $R^{5*}$ ,  $R^{6*}$ ,  $R^{7*}$ , and  $R^{8*}$  are as defined above. In some embodiments,  $R^{5*}$  is H and, each of  $R^{2*}$ ,  $R^{3*}$ ,  $R^{4*}$ ,  $R^{6*}$ ,  $R^{7*}$ , and  $R^{8*}$  are OH.

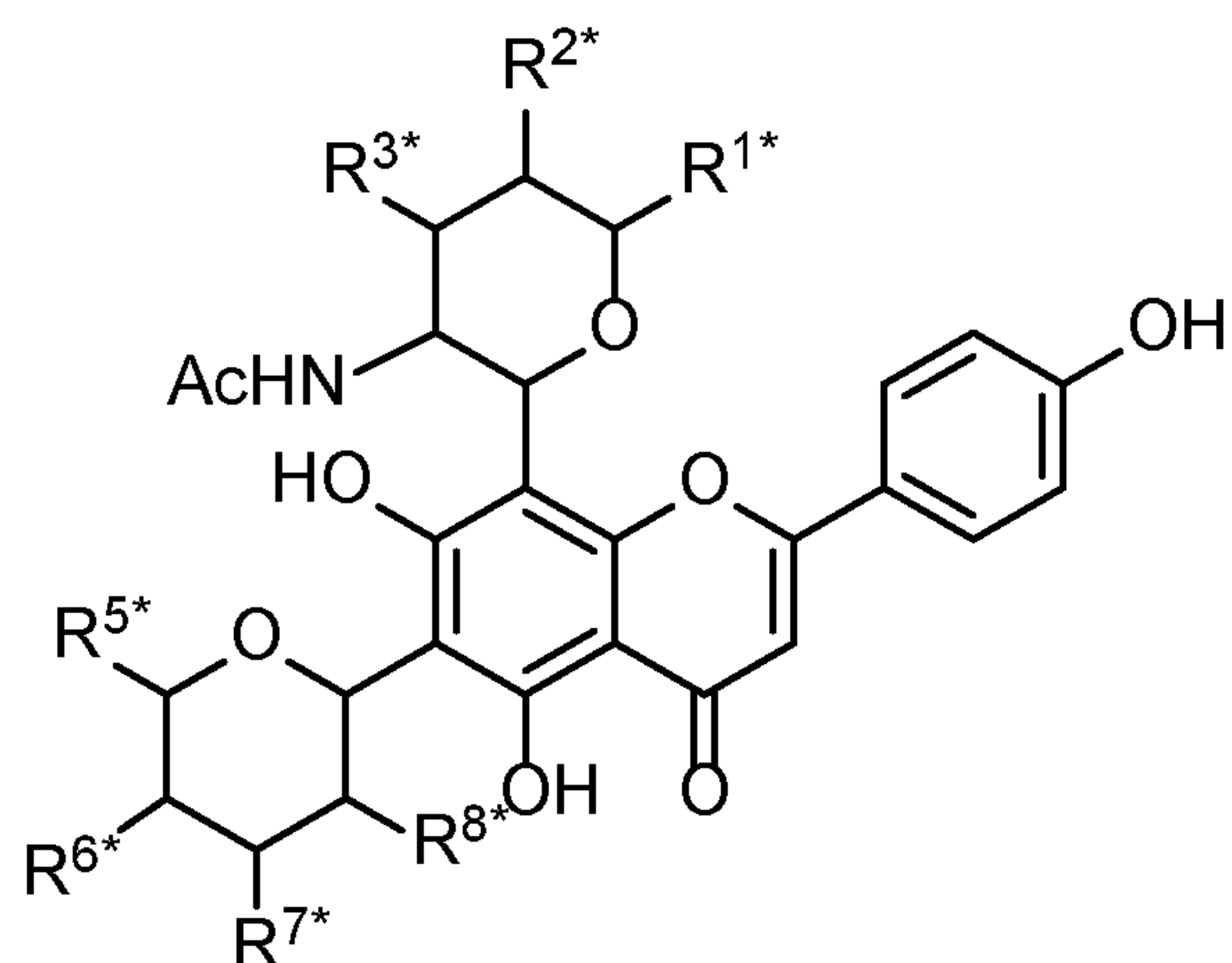
In some instances, the flavor modulating compound has the formula:



5

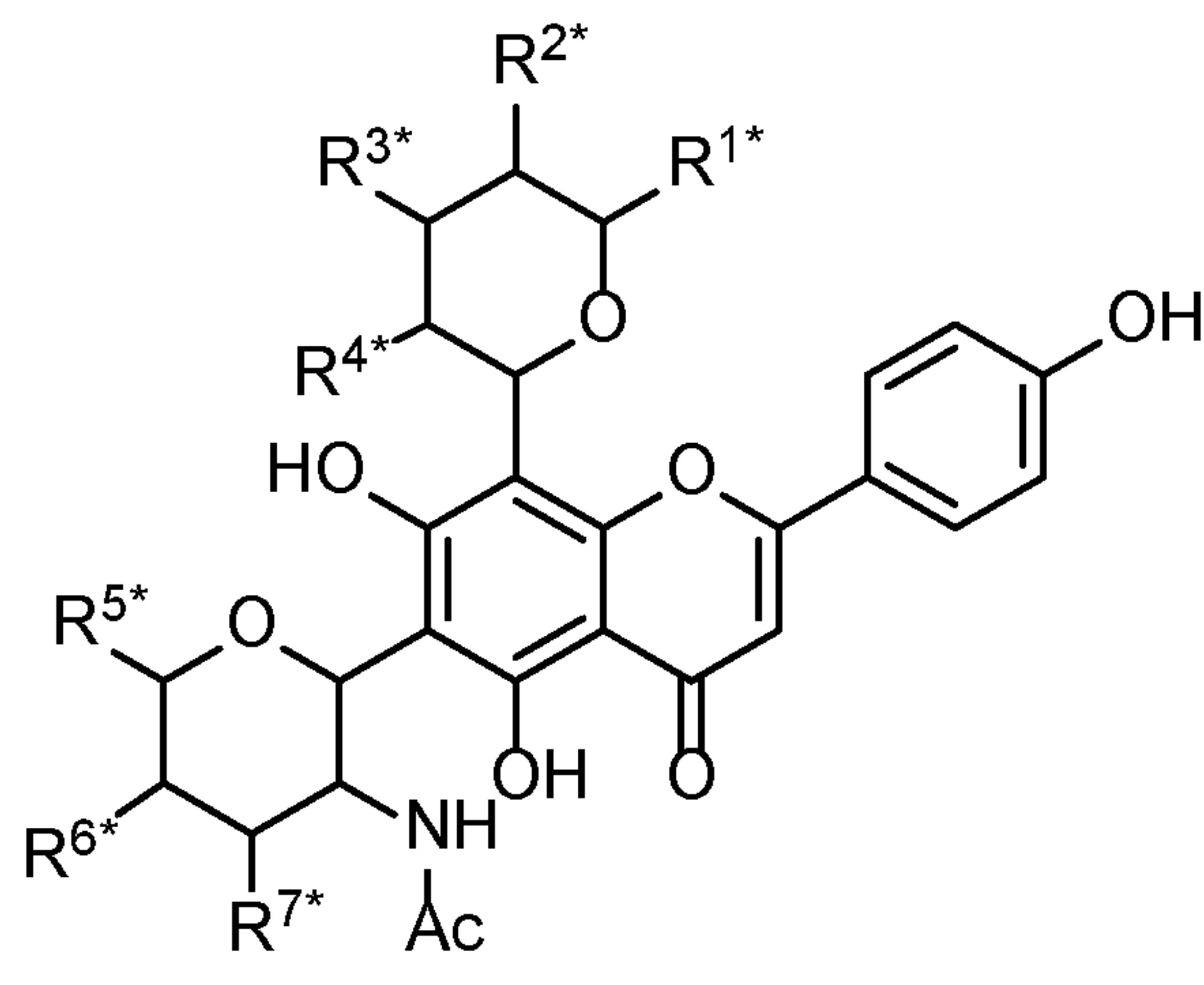
wherein  $R^{1*}$ ,  $R^{2*}$ ,  $R^{3*}$ ,  $R^{4*}$ ,  $R^{6*}$ ,  $R^{7*}$ , and  $R^{8*}$  are as defined above. In some embodiments,  $R^{1*}$  is  $\text{CH}_2\text{OH}$  and each of  $R^{2*}$ ,  $R^{3*}$ ,  $R^{4*}$ ,  $R^{6*}$ ,  $R^{7*}$ , and  $R^{8*}$  are OH.

In some instances, the flavor modulating compound has the formula:



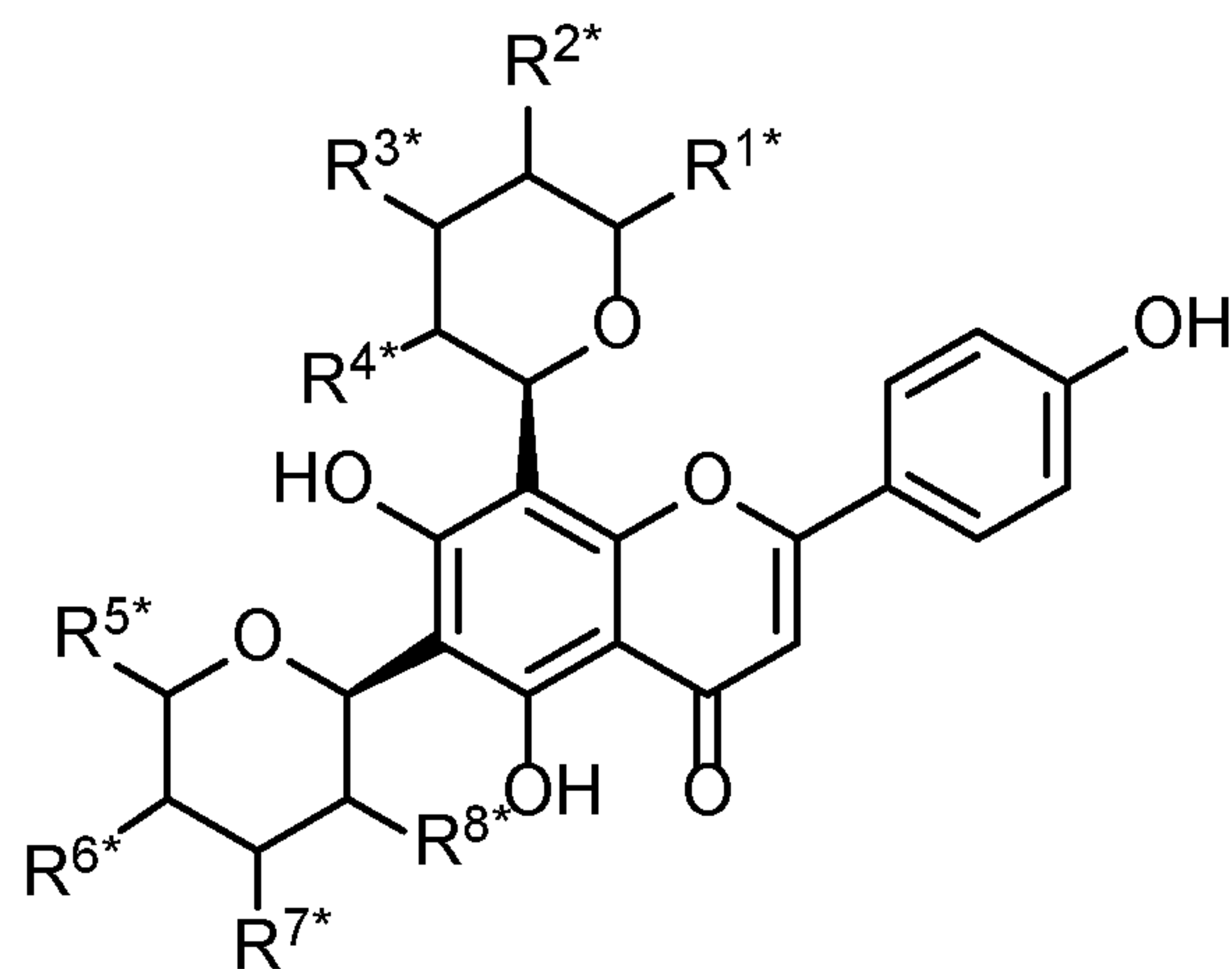
10 wherein  $R^{1*}$ ,  $R^{2*}$ ,  $R^{3*}$ ,  $R^{4*}$ ,  $R^{5*}$ ,  $R^{6*}$ ,  $R^{7*}$ , and  $R^{8*}$  are as defined above. In some embodiments,  $R^{1*}$  is  $\text{CH}_2\text{OH}$ ,  $R^{5*}$  is H, and each of  $R^{2*}$ ,  $R^{3*}$ ,  $R^{4*}$ ,  $R^{6*}$ ,  $R^{7*}$ , and  $R^{8*}$  are OH.

In some instances, the flavor modulating compound has the formula:



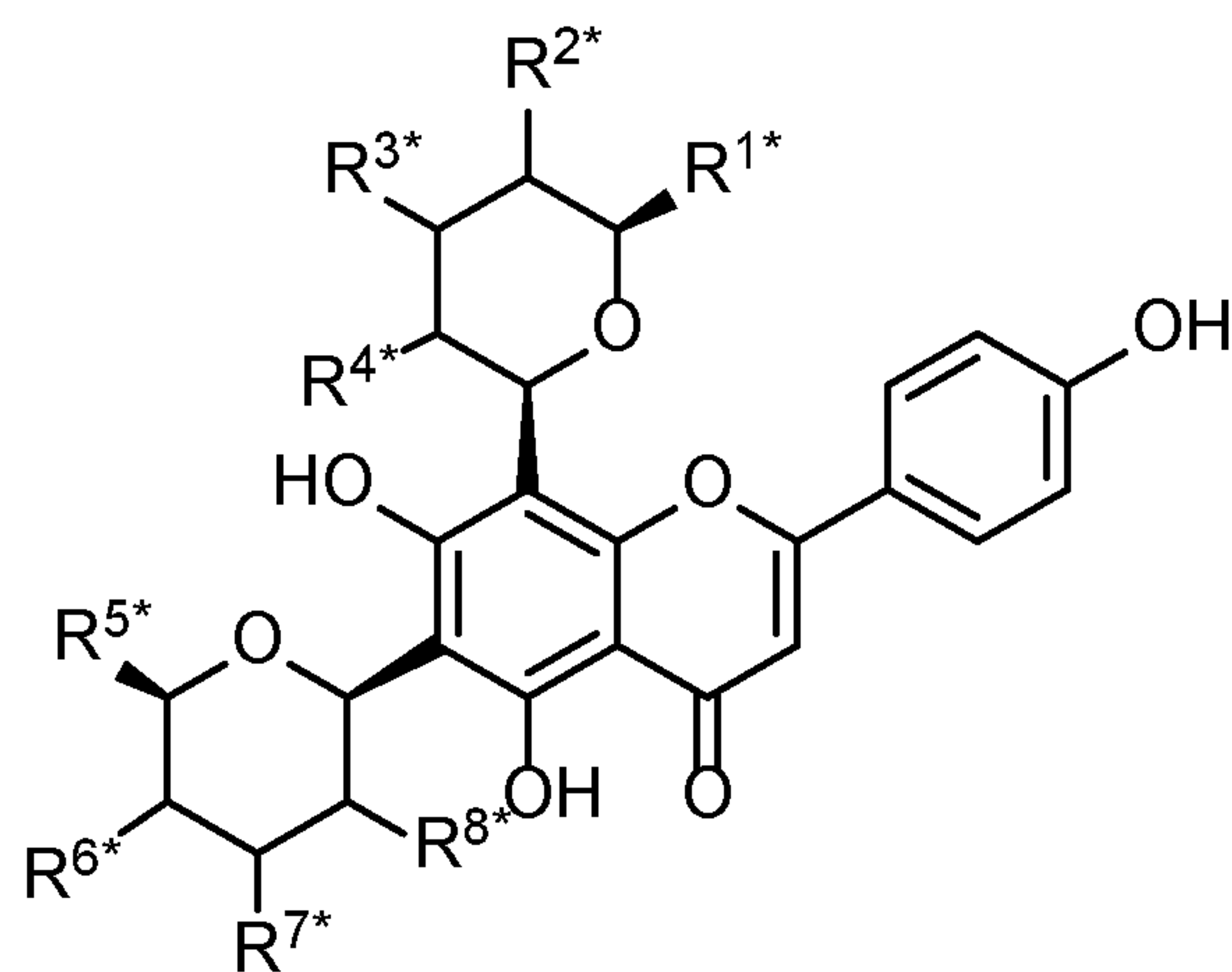
wherein  $R^{1*}$ ,  $R^{2*}$ ,  $R^{3*}$ ,  $R^{4*}$ ,  $R^{5*}$ ,  $R^{6*}$ , and  $R^{7*}$  are as defined above. In some embodiments,  $R^{1*}$  is  $CH_2OH$ ,  $R^{5*}$  is H, and each of  $R^{2*}$ ,  $R^{3*}$ ,  $R^{4*}$ ,  $R^{5*}$ ,  $R^{6*}$ , and  $R^{7*}$  are OH.

5 In some instances, the flavor modulating compound can have the formula:



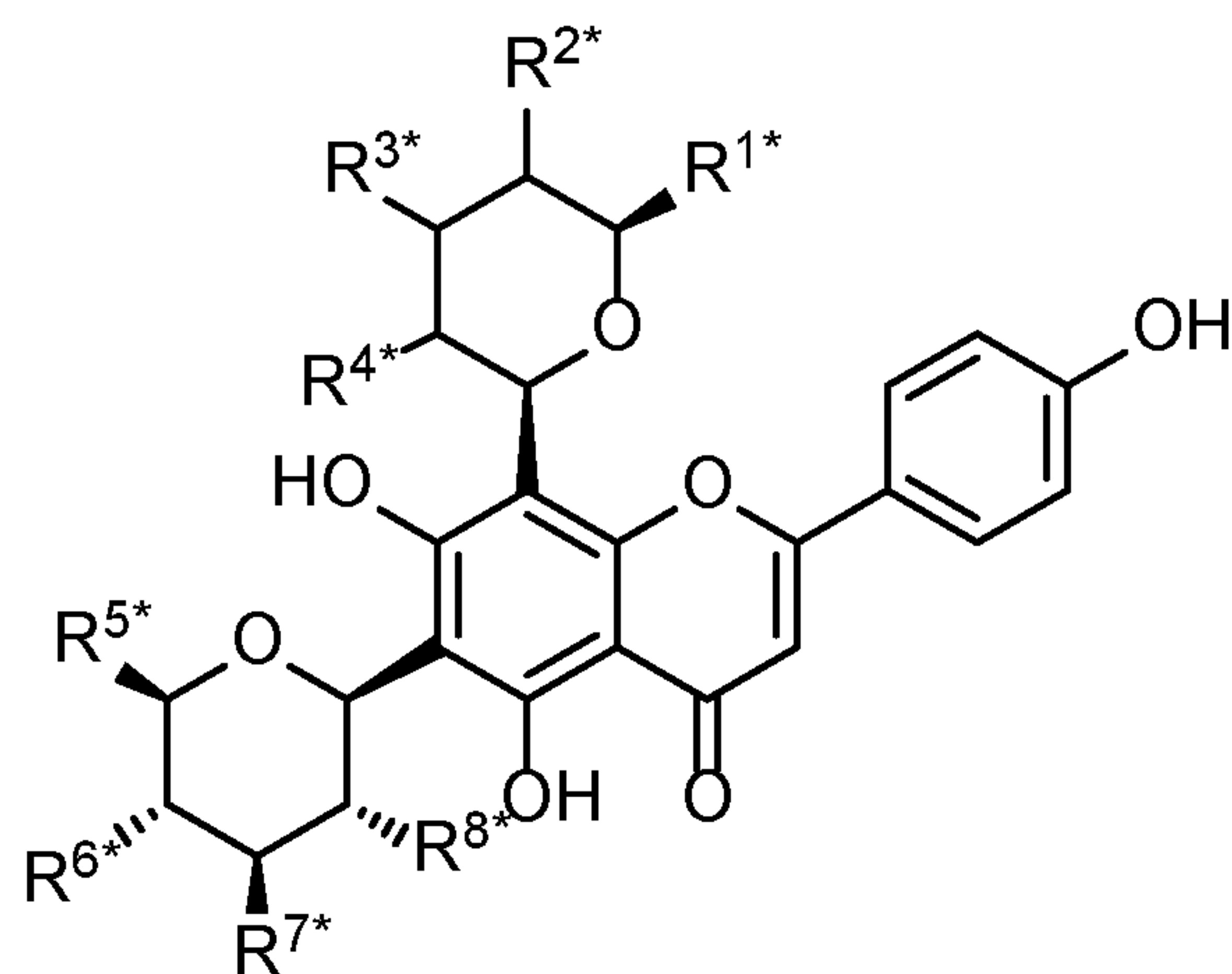
wherein  $R^{1*}$ ,  $R^{2*}$ ,  $R^{3*}$ ,  $R^{4*}$ ,  $R^{5*}$ ,  $R^{6*}$ ,  $R^{7*}$ , and  $R^{8*}$  are as defined above.

In some instances, the flavor modulating compound can have the formula:



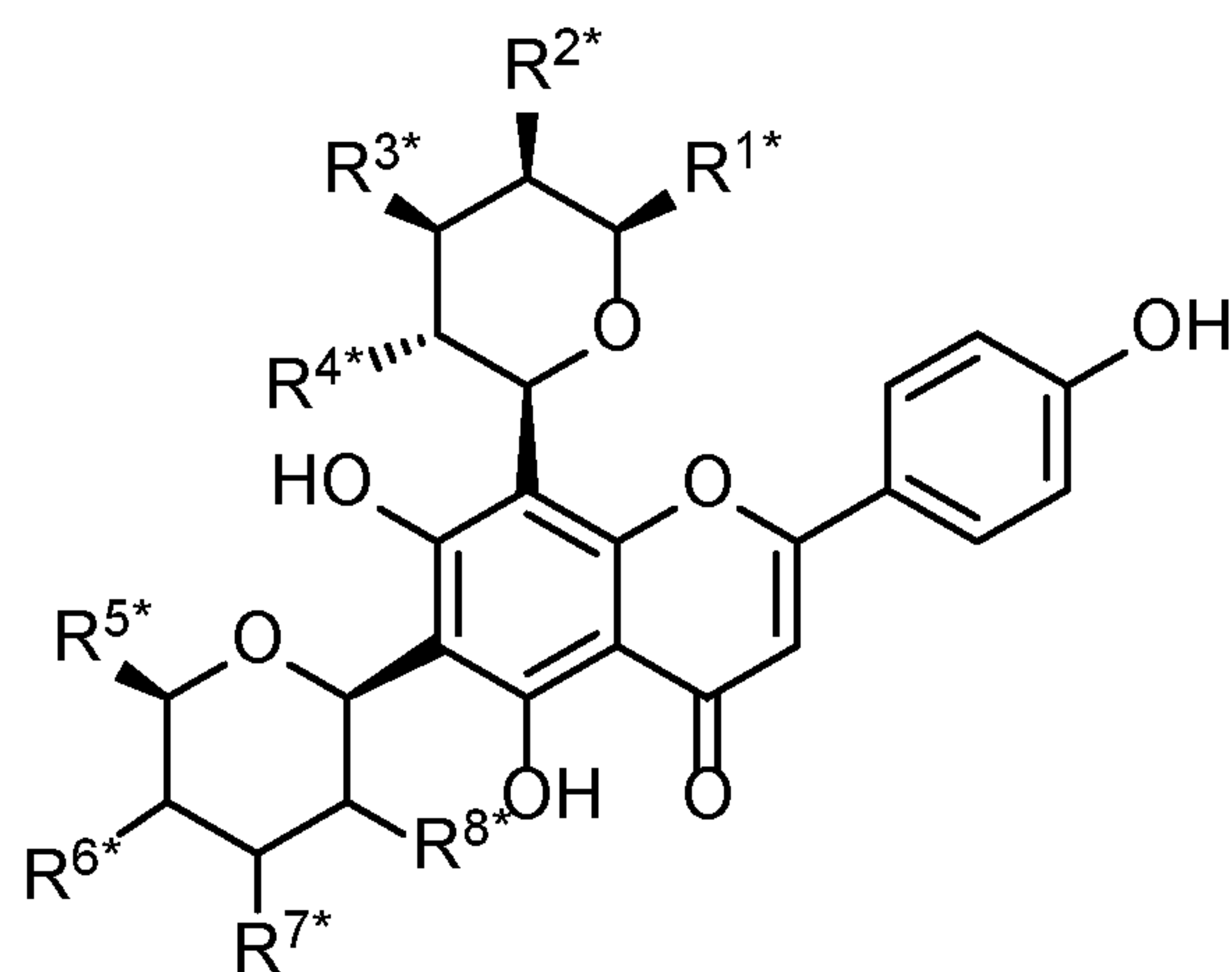
10 wherein  $R^{1*}$ ,  $R^{2*}$ ,  $R^{3*}$ ,  $R^{4*}$ ,  $R^{5*}$ ,  $R^{6*}$ ,  $R^{7*}$ , and  $R^{8*}$  are as defined above.

In some instances, the flavor modulating compound can have the formula:



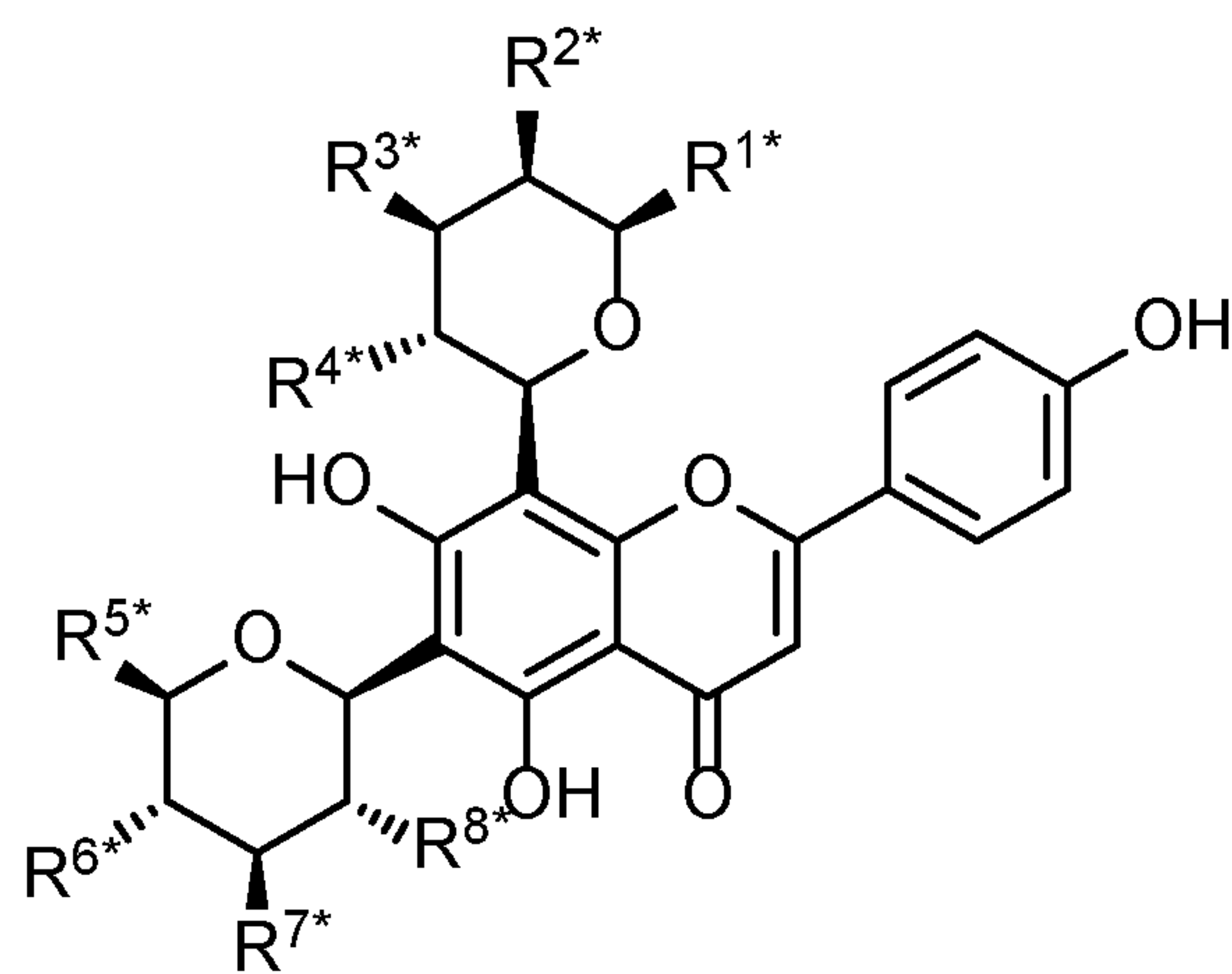
wherein  $R^{1*}$ ,  $R^{2*}$ ,  $R^{3*}$ ,  $R^{4*}$ ,  $R^{5*}$ ,  $R^{6*}$ ,  $R^{7*}$ , and  $R^{8*}$  are as defined above.

In some instances, the flavor modulating compound can have the formula:



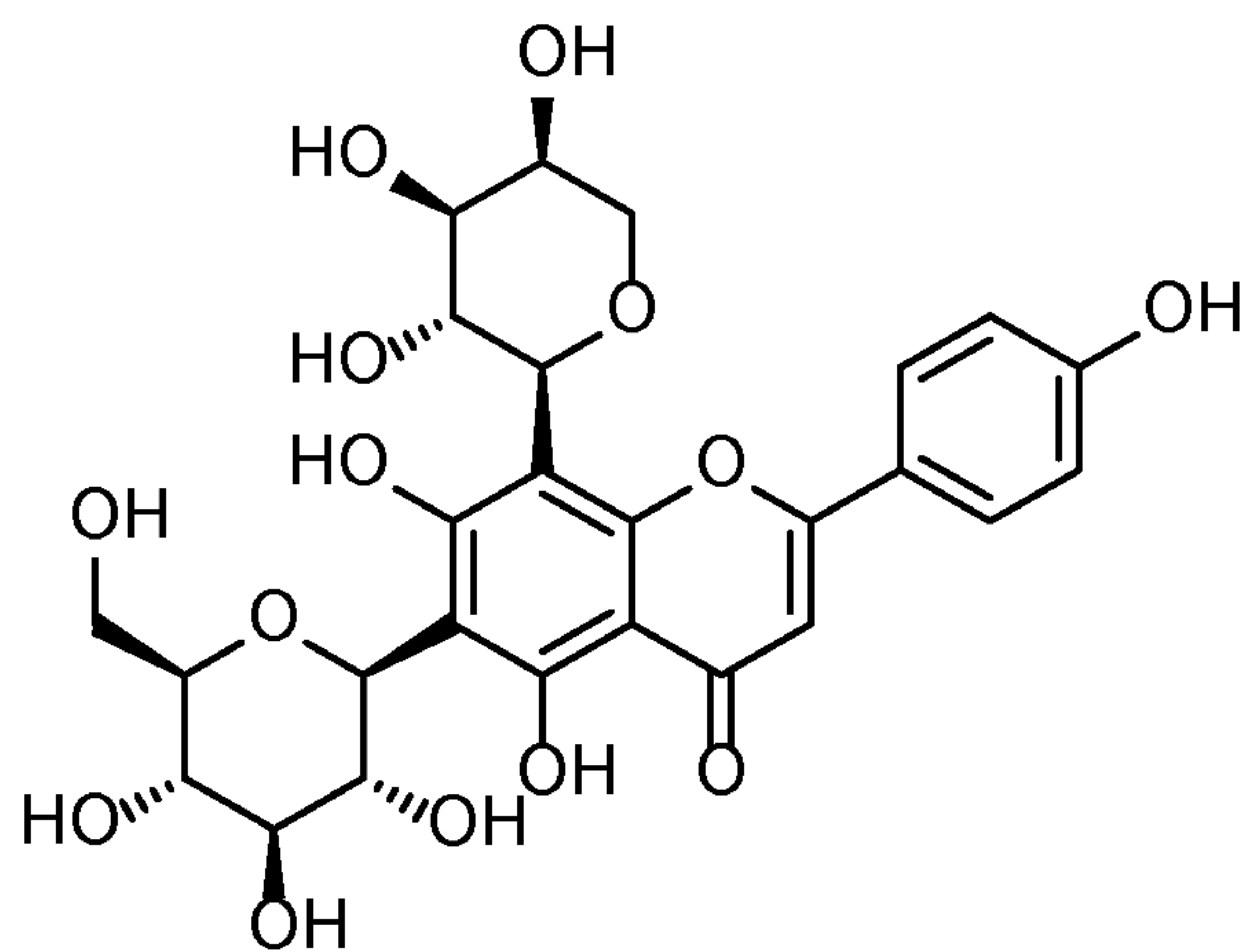
5 wherein  $R^{1*}$ ,  $R^{2*}$ ,  $R^{3*}$ ,  $R^{4*}$ ,  $R^{5*}$ ,  $R^{6*}$ ,  $R^{7*}$ , and  $R^{8*}$  are as defined above.

In some instances, the flavor modulating compound can have the formula:



wherein  $R^{1*}$ ,  $R^{2*}$ ,  $R^{3*}$ ,  $R^{4*}$ ,  $R^{5*}$ ,  $R^{6*}$ ,  $R^{7*}$ , and  $R^{8*}$  are as defined above.

In some instances the flavor modulating compound is schaftoside, having the formula:



The flavor modulating compounds may be added to foods and beverages in concentrations effective to block the bitter and/or sour tastes of the compounds contained therein. The compounds can augment or improve flavors as well as somatosensory effects (e.g., warming cooling sensations) in foods and beverages. The flavor modulating compounds can improve and/or augment the aromas associated with a particular food or beverage. In preferred embodiments, the flavor modulating compounds can be added to a food product such as a grain product. A preferred grain product is flour or dough. In certain embodiments, the food product is beer, wine, distilled spirit or precursor thereof (e.g., mash, grist, grain bill, wort, etc). In yet further embodiments, the food product is a cereal (i.g., oats, barley, rye, rice), tubers (e.g., potatoes, etc.), vegetables (e.g., arugula, kale, broccoli, cabbage, radishes, brussels sprouts), legumes (e.g., peas, soy, etc.) and nuts (e.g., hazelnuts), among others. In other embodiments, the food product is mechanically deboned meat and meat products can also generate pinellic acid.

The compounds may be added to food products as a pure compound (or mixture of compounds), or they may be added as part of an extract or crude mixture having a sufficient content of flavor modulating compound. For example, wheat and other grain products may be subjected to series of extractive protocols to provide an enriched composition of flavor modulating compounds.

For instance, the disclosed compounds may be added in an amount of at least 0.1 mg/kg, at least 0.5 mg/kg, at least 1 mg/kg, at least 2.5 mg/kg, at least 5 mg/kg, at least 10 mg/kg, at least 20 mg/kg, at least 30 mg/kg, at least 40 mg/kg, at least 50 mg/kg, at least 60 mg/kg, at least 70 mg/kg, at least 80 mg/kg, at least 90 mg/kg, at least 100 mg/kg, at least 200 mg/kg, at least 300 mg/kg, at least 400 mg/kg, at least 500 mg/kg, or at least 1,000 mg/kg relative to the total weight of the food product. In some embodiments, the flavor modulating compound can be added in an amount from 0.1-100 mg/kg, from 25-125 mg/kg, from 50-200

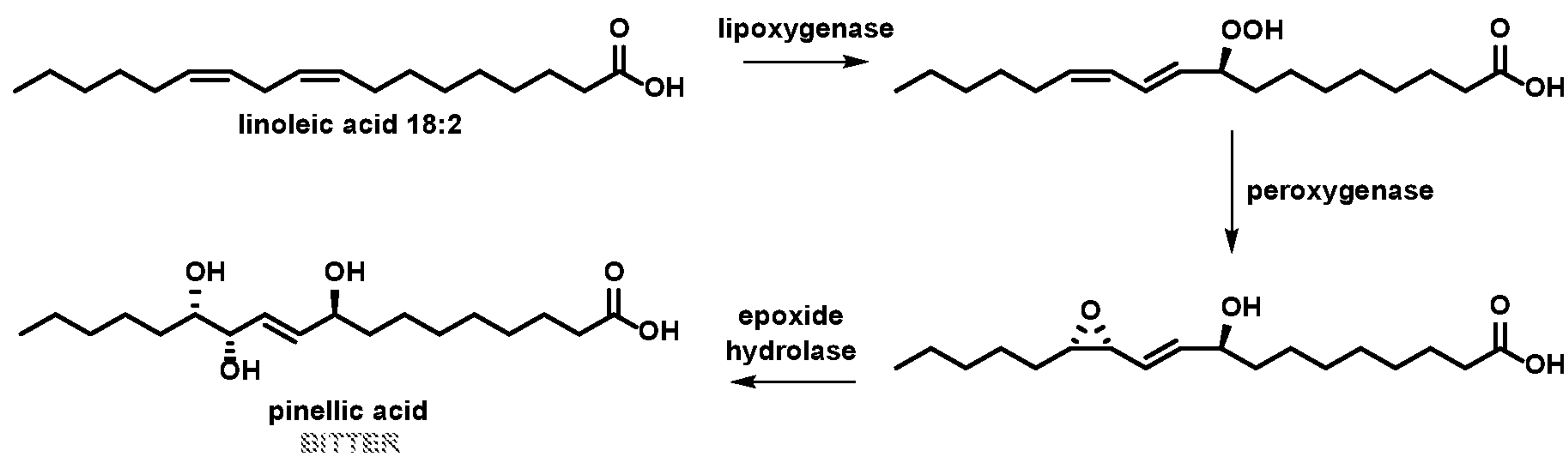
mg/kg, from 100-500 mg/kg, or from 250-1,000 mg/kg, relative to the total weight of the food product.

In certain embodiments, the flavor modulating compounds can be delivered to the oral cavity prior to consumption of the bitter product. The compounds can be formulated as a mouthwash, a lozenge, a lollipop, a chewable tablet, and the like. By pre-saturating the bitter and/or sour taste receptors in the tongue with the flavor modulating compounds, otherwise unpalatable substances may be more readily delivered to the oral cavity or consumed.

The compounds disclosed herein may be provided in an aqueous composition to more readily combine them with foods, beverages, and the like. The composition may be buffered, for instance at a pH between 6 and 8, between 6.5 and 8, between 6.5 and 7, between 6.5 and 7.5, between 6.5 and 8, between 7 and 8, or between 7.5 and 8. In other embodiments, the composition may be buffered at an acidic pH, for instance similar to found in citrus juice, vinegar, or yogurt. In some embodiment, the composition may be buffered at a pH between 2 and 8, between 2 and 7, between 2 and 6, between 2 and 5, between 2 and 4, between 3 and 8, between 3 and 7, between 3 and 6, between 3 and 5, between 3 and 4, between 4 and 8, between 4 and 7, between 4 and 6, between 4 and 5, between 5 and 8, between 5 and 7, or between 5 and 6.

The compounds may be provided in the composition at a concentration between about 0.1 – 100 mM, between about 0.5 – 100 mM, between about 1 – 100 mM, between about 5 – 100 mM, between about 10 – 100 mM, between about 25 – 100 mM, between about 50 – 100 mM, between about 0.1 – 50 mM, between about 0.1 – 25 mM, between about 0.1 – 10 mM, between about 0.1 – 5 mM, or between about 0.1 – 1 mM. When the aqueous composition contains more than one flavor modulating compound, the concentration refers to the total concentration of all the compounds.

It has been discovered that the bitter flavors found in whole grain foods are associated with the occurrence of pinellic acid. The dominant route for the formation of pinellic acid is through an enzymatic oxidation pathway in which the initial substrate, linoleic acid is sequentially converted to its trihydroxylated form, pinellic acid (Scheme 1).



Thus, disclosed herein are compounds capable of reducing pinellic acid levels in food products. In some instances, addition of the compounds disclosed herein to food precursors can reduce pinellic acid levels by at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 40%, at least 50% relative to when the compounds are not added. Exemplary food precursors include flour, dough, and alcoholic beverage precursors as described above.

## EXAMPLES

The following examples are for the purpose of illustration of the invention only and are not intended to limit the scope of the present invention in any manner whatsoever.

For the dough analysis 15 mg of Hard Red Winter (“HRW”) Everest flour was weighed into 2 Eppendorf tubes containing one ¼ inch stainless steel balls, followed by the addition of 12 µL of water (4:5 water/flour ratio) to make a control dough sample. The treatment dough sample was similarly prepared to the control sample with the exception that 946.5 ng of Schaftoside in 12 µL of water (4:5 water/flour ratio) was added instead of pure water.

The concentration of pinellic acid was analyzed for both control and treatment dough samples using the following method: The 15 mg of dough (or 27mg of bread) was extracted with 1 mL 1:1 IPA/H<sub>2</sub>O (v/v) spiked with prostaglandin-F<sub>2</sub>α (PGE-f<sub>2</sub>α) ISTD. Samples were sonicated for 10 min followed by shaking using the GenoGrinder at 1000 rpm for 10 min. Samples were then diluted 1:50 and sample clean-up was carried out using a 96-well Oasis PRiME HLB plate (1 cc, 30 mg sorbent). After sample load (250 µL) and wash (750 µL, 10% acetonitrile (aq.) with 0.1% formic acid) steps, the retentate was eluted with 500 µL 90% acetonitrile (aq.) with 0.1% formic acid. Samples were further diluted to 2 mL using water with 0.1% formic acid. The standard calibration curve was prepared using 6-points ranging from 0.24 ng/mL to 500 ng/mL.

Quantitative analysis was conducted using MRM acquisition. LC/MS/MS analysis was conducted using a Waters ACQUITY H-class UPLC system coupled with a Xevo TQ-S mass

spectrometer (Waters Co.). Conditions employed included a capillary voltage of 2.2 kV, sample cone voltage of 50V, ESI<sup>+</sup>, a source temperature of 150°C, and a desolvation temperature of 550 °C. Chromatographic separation was performed on an ACQUITY UPLC BEH C18 1.7 µm column (2.1 mm × 50 mm) (Waters Co.) kept at 40 °C. Nanopure water with 0.1% formic acid (solvent A) and 9:1 acetonitrile/isopropanol with 0.1% formic acid (solvent B) were used for the mobile phase. Flow rate was set to 0.5 mL/min and a solvent gradient program of 25% B (0.0 – 1.0 min), 25-95% B (1.0 – 8.0 min), 95% B (8.0 - 8.5 min), 25% B (8.5 – 10.0 min) was employed. The MS/MS transitions and collision energy for pinellic acid was ESI<sup>+</sup>  $m/z$  329 → 211 and 22 eV, for PGE-f2α was  $m/z$  353 → 193 (22 eV).

Wheat breads were made using a modified AACC straight-dough bread-making method (AACC, 1999). The control bread formula (based on 200 g flour) included 200 g of whole wheat flour, 10.6 g of dry yeast, 12 g of sugar, 3 g of salt, 6 g of shortening, and 164 g of water. Ingredients were mixed using a dough mixer (KitchenAid, Benton Harbor, MI) until a sponge dough was formed, approximately 2.5 min. The dough was moved into a 5-3/4" x 3-1/4" x 2-1/4" loaf pan and fermented for 52 min at 30 °C and 85% relative humidity, then proofed for 25 min and 33 min. Finally, the fermented dough was baked at 215 °C with a beaker filled with 1 L of water for 17 min. Yeast, salt, shortening, and sugar were obtained from the local grocery store (Columbus, OH USA). A treatment bread sample was prepared similarly to the control sample, with the exception that rather than using pure water to make the dough, a water solution with schaftoside was used instead to increase the amount of schaftoside from 88.4 mg/kg to 151.5 mg/kg (an increase of 68.1 mg/kg flour). Sample preparation was as follows; 27 mg of bread was weighed into 2 Eppendorf tubes containing one ¼ inch stainless steel balls. The concentration of pinellic acid was analyzed for both control and spiking whole wheat bread samples as described for the dough analysis. The treatment bread sample was significantly lower (pvalue<0.05) in pinellic acid at 228.6 mg/kg compared to the control bread sample at 308.64 mg/kg; thus a 26% reduction in pinellic acid formation resulted from the addition of Schaftoside to the flour prior to bread making. Figure 1. Similarly, the treatment dough sample reported a significant (pvalue<0.05) 30% reduction in pinellic acid content compared to the control bread sample, which was aligned with the results of whole wheat bread.

Twenty participants were recruited by Flavor Research and Education Center (FREC) at The Ohio State University. The whole wheat bread samples (control and treatment) were cut into 3 cm × 2 cm × 1 cm (L×W×H) squares of crumb the day before the test and stored at room temperature in sealed 2 oz cups labeled with a 3-digit codes. Each panelist evaluated one

pair of samples containing the control sample and the treatment sample. Panelists used nose clips during the evaluation in order to prevent interactions with olfactory responses. Panelists were instructed to place the entire piece of bread crumb in their mouth, chew for 10 seconds, and evaluate the maximum bitter intensity perceived. After evaluating each sample in the pair, panelists were asked to choose the most bitter sample. The serving order of each bread sample was balanced. Water was used as a palate cleanser.

Compusense Cloud Software version 7.2 (Compusense, Guelph, Canada) was used for data collection. Approval of the sensory evaluation protocol was granted by the Ethics Committee, The Ohio State University (IRB # 2019B0402). Paired Student t-tests was executed with SPSS Statistics Version 25 (International Business Machines Corp., Armonk, NY). Sensory difference testing indicated the treatment bread sample was significantly less bitter ( $P\text{value} < 0.05$ ) than the control bread sample. Thus, the addition of schaftoside to the flour prior to bread making suppressed the generation of pinellic acid that resulted in a reduced perceived bitterness intensity of whole wheat bread.

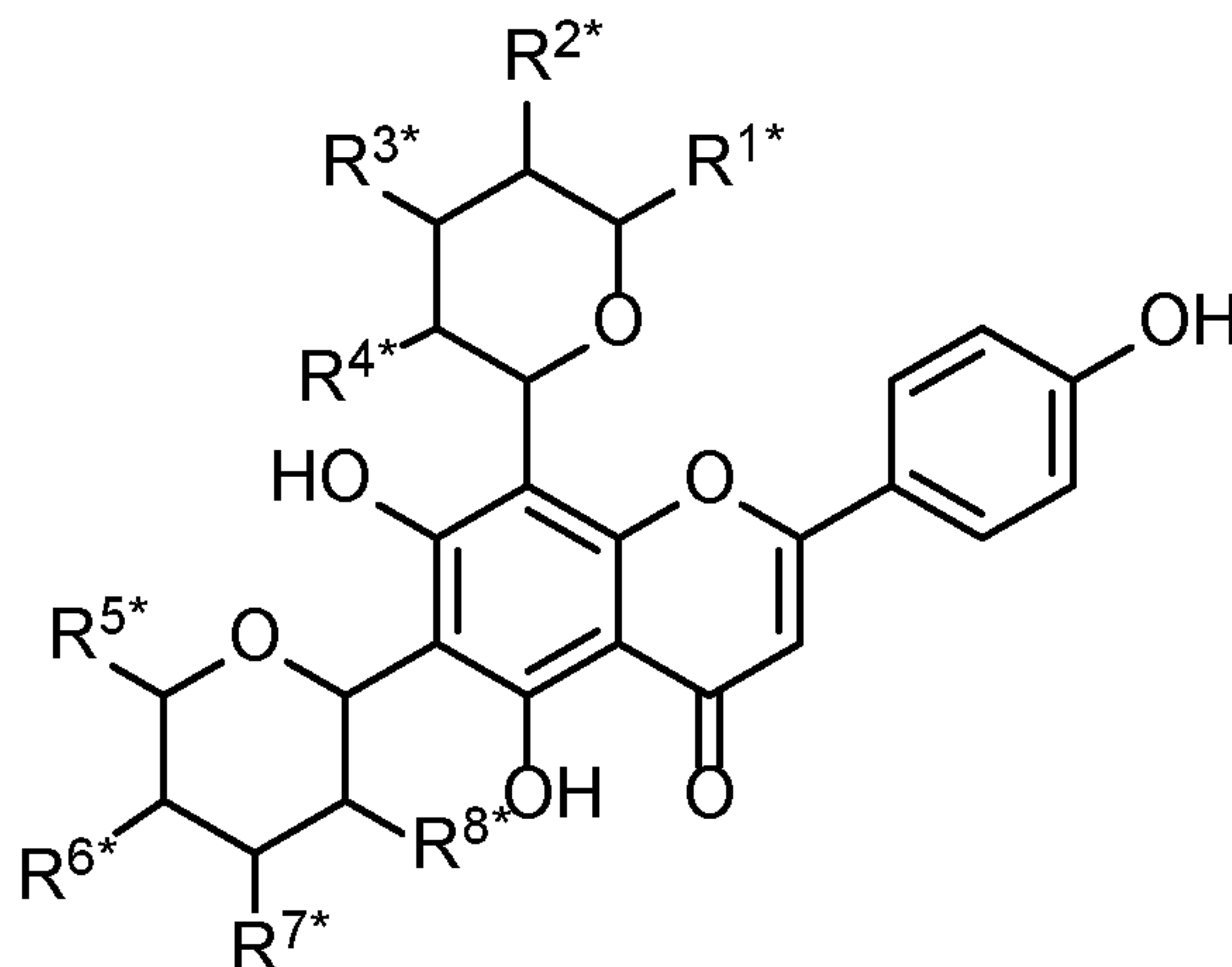
The compositions and methods of the appended claims are not limited in scope by the specific compositions and methods described herein, which are intended as illustrations of a few aspects of the claims and any compositions and methods that are functionally equivalent are intended to fall within the scope of the claims. Various modifications of the compositions and methods in addition to those shown and described herein are intended to fall within the scope of the appended claims. Further, while only certain representative compositions and method steps disclosed herein are specifically described, other combinations of the compositions and method steps also are intended to fall within the scope of the appended claims, even if not specifically recited. Thus, a combination of steps, elements, components, or constituents may be explicitly mentioned herein or less, however, other combinations of steps, elements, components, and constituents are included, even though not explicitly stated. The term “comprising” and variations thereof as used herein is used synonymously with the term “including” and variations thereof and are open, non-limiting terms. Although the terms “comprising” and “including” have been used herein to describe various embodiments, the terms “consisting essentially of” and “consisting of” can be used in place of “comprising” and “including” to provide for more specific embodiments of the invention and are also disclosed. Other than in the examples, or where otherwise noted, all numbers expressing quantities of ingredients, reaction conditions, and so forth used in the specification and claims are to be understood at the very least, and not as an attempt to limit the application of the doctrine of

equivalents to the scope of the claims, to be construed in light of the number of significant digits and ordinary rounding approaches.

## CLAIMS

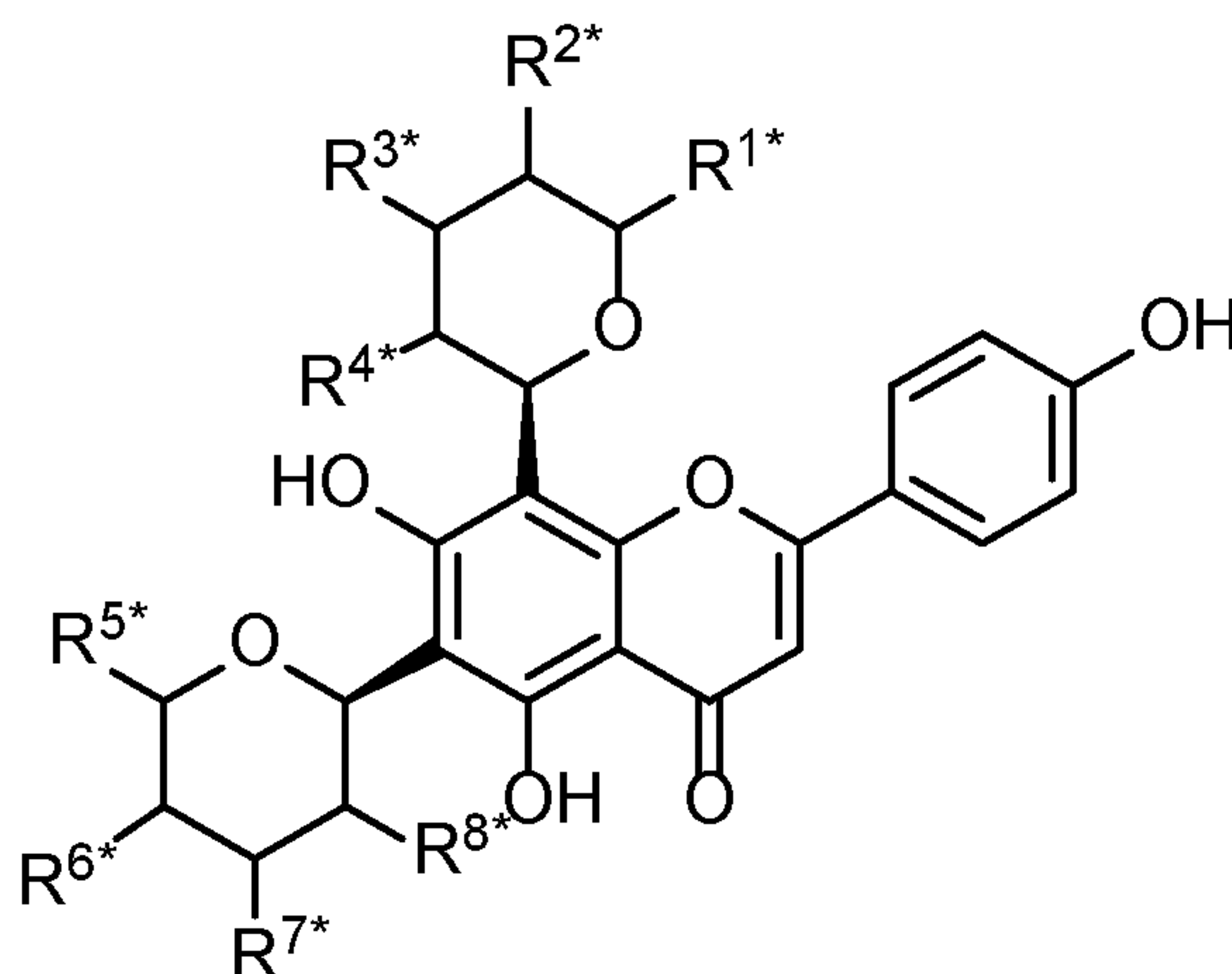
What is claimed is:

1. A method for modulating the flavor of a food product, comprising adding to the food product a compound having the formula:

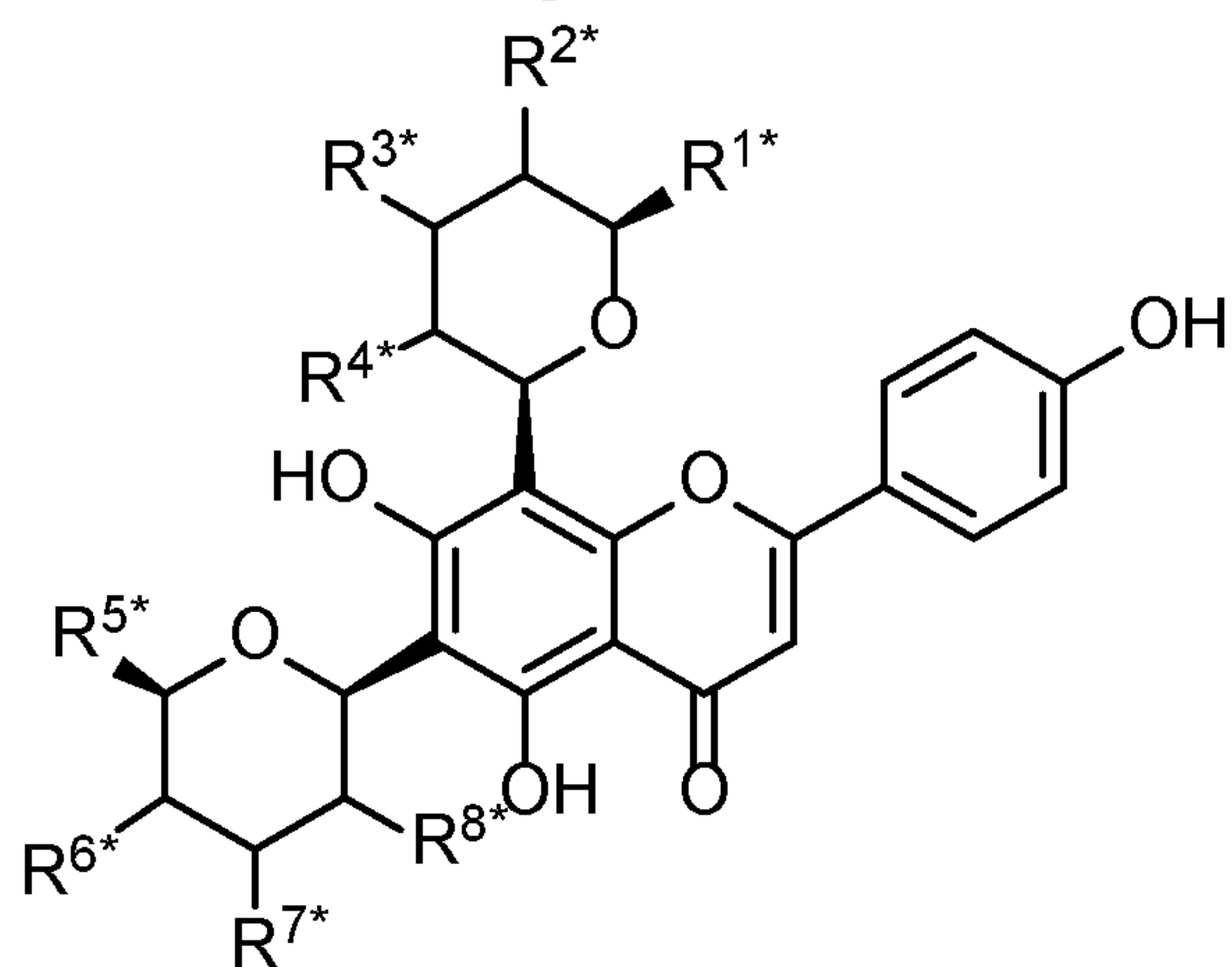


wherein R<sup>1\*</sup>, R<sup>2\*</sup>, R<sup>3\*</sup>, R<sup>4\*</sup>, R<sup>5\*</sup>, R<sup>6\*</sup>, R<sup>7\*</sup>, and R<sup>8\*</sup> are independently selected from H, (CH<sub>2</sub>)<sub>n</sub>OH, OC(O)C<sub>1-8</sub>alkyl, NHC(O)CH<sub>3</sub>, CO<sub>2</sub>H, NH<sub>2</sub>, O-C<sub>1-8</sub>alkyl, wherein n is selected from 0 or 1.

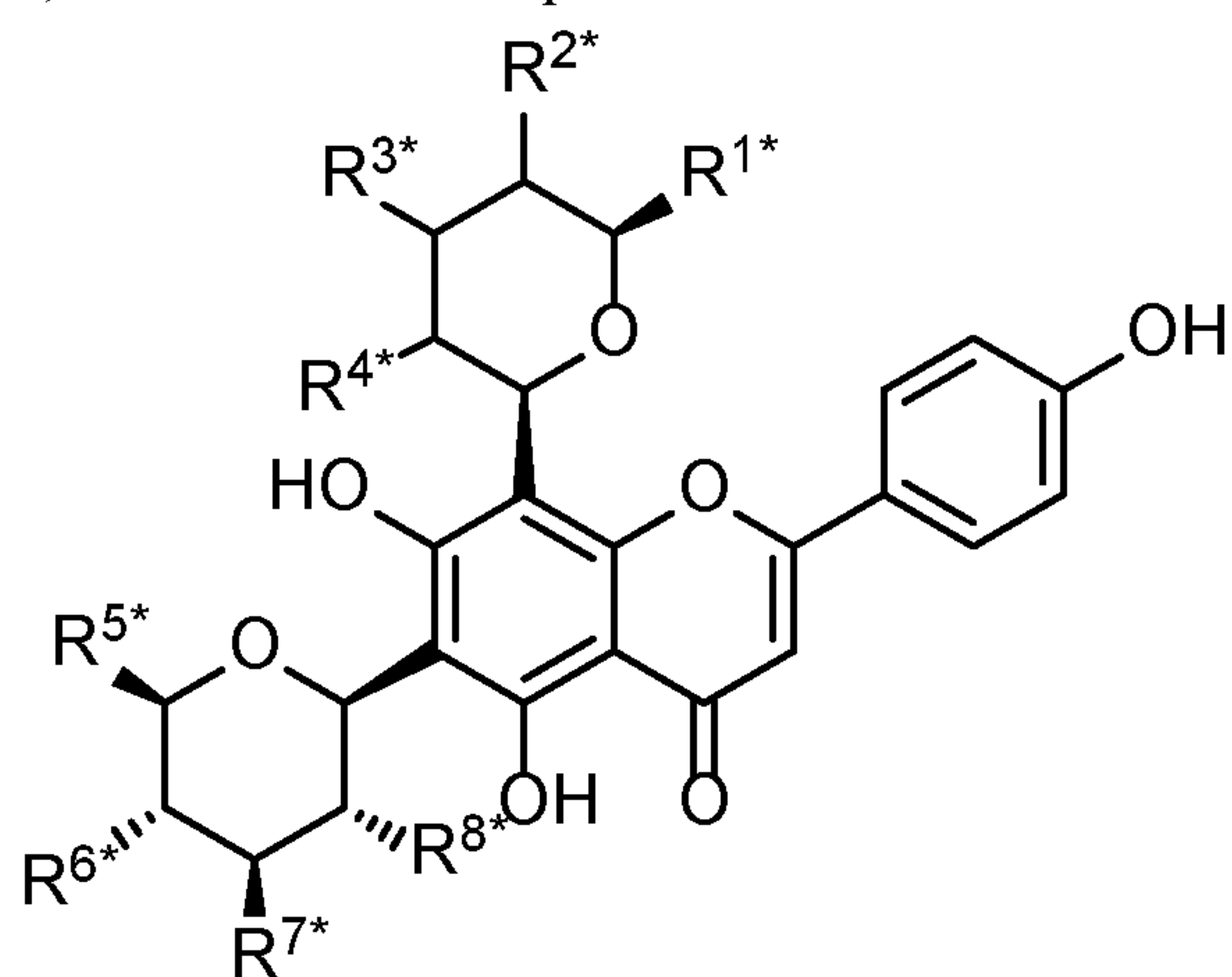
2. The method of claim 1, wherein the compound has the formula:



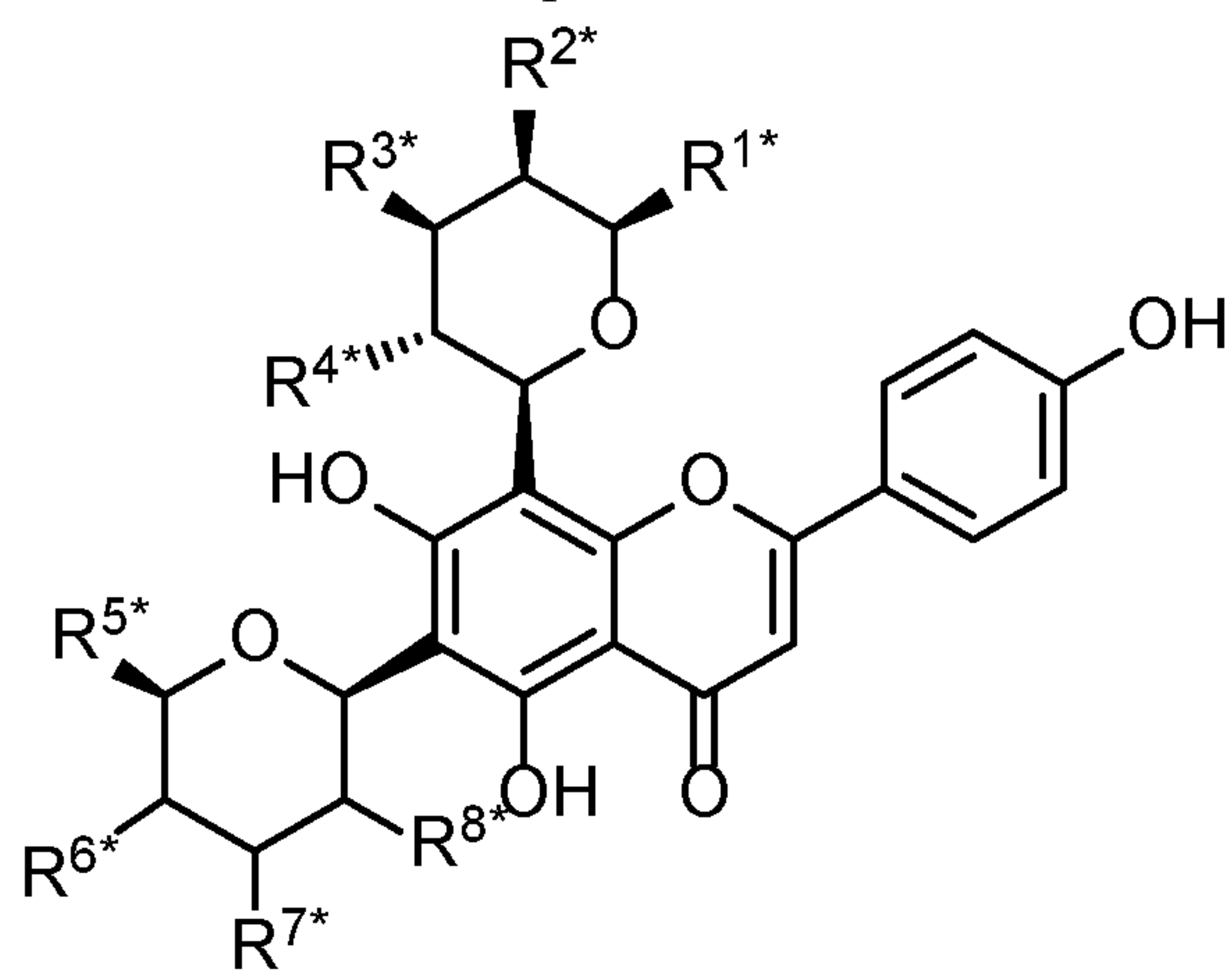
3. The method of claim 1, wherein the compound has the formula:



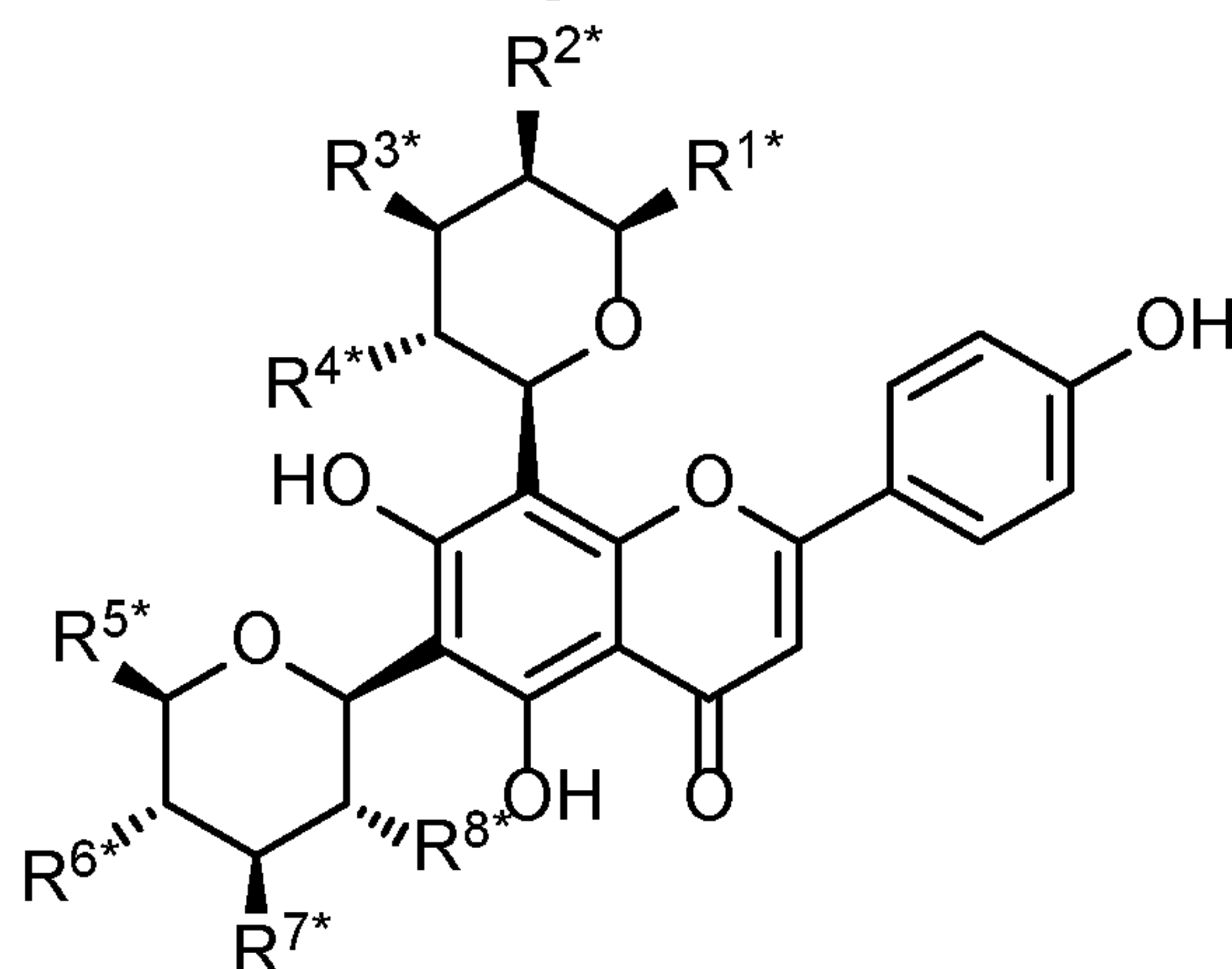
4. The method of claim 1, wherein the compound has the formula:



5. The method of claim 1, wherein the compound has the formula:



6. The method of claim 1, wherein the compound has the formula:



7. The method of any of claims 1-6, wherein  $R^{1*}$  is  $CH_2OH$ ,  $R^{5*}$  is H, and each of  $R^{2*}$ ,  $R^{3*}$ ,  $R^{4*}$ ,  $R^{6*}$ , and  $R^{7*}$  are OH.

8. The method of any of claims 1-6, wherein R<sup>1\*</sup> is CO<sub>2</sub>H.

9. The method of any of claims 1-6, wherein R<sup>5\*</sup> is CO<sub>2</sub>H.

10. The method of any of claims 1-6, wherein  $R^{4*}$  is  $NHC(O)CH_3$ .

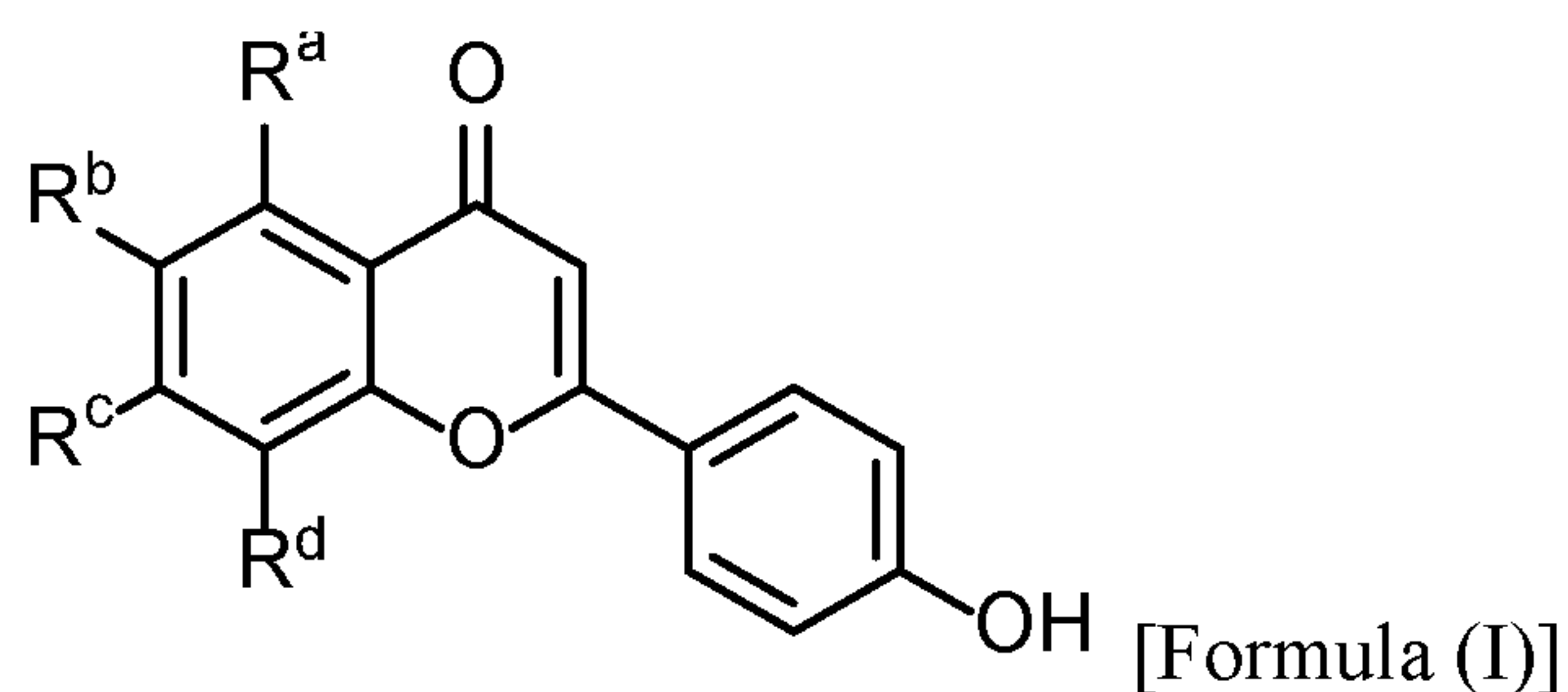
11. The method of any of claims 1-6, wherein  $R^{8*}$  is  $NHC(O)CH_3$ .

12. The method of claim 7, wherein the compound is added in an amount of at least 100 mg/kg, relative to the total weight of the food product.

13. The method according to any of claims 1-6, wherein the food product is a grain.

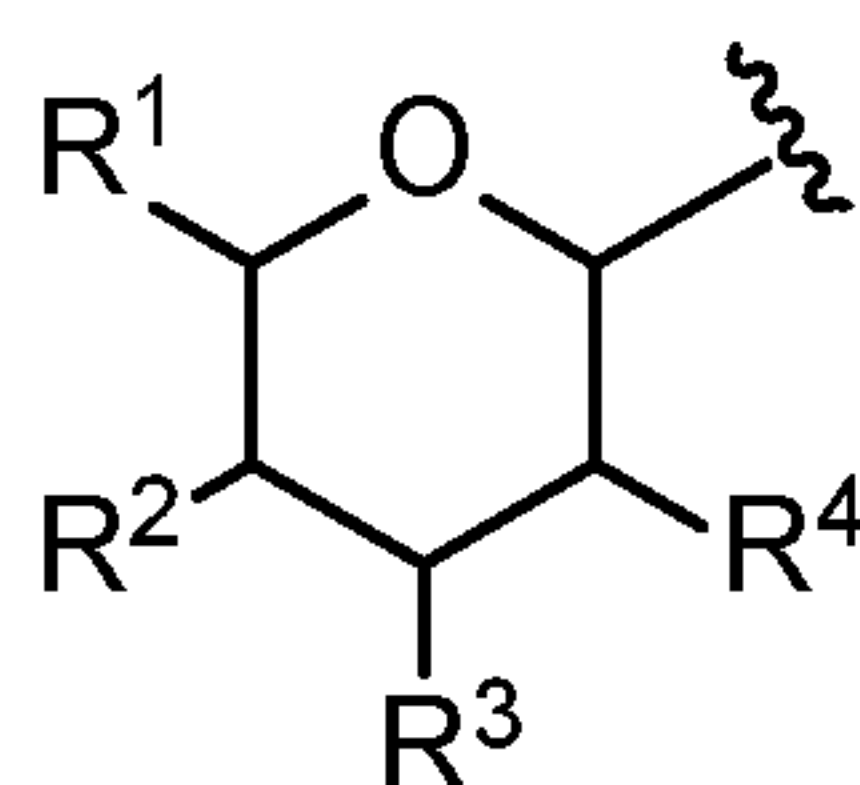
14. The method according to any of claims 1-6, wherein the food product is flour or dough.

15. A method for modulating the flavor of a food product, comprising adding to the food product a compound of Formula (I):

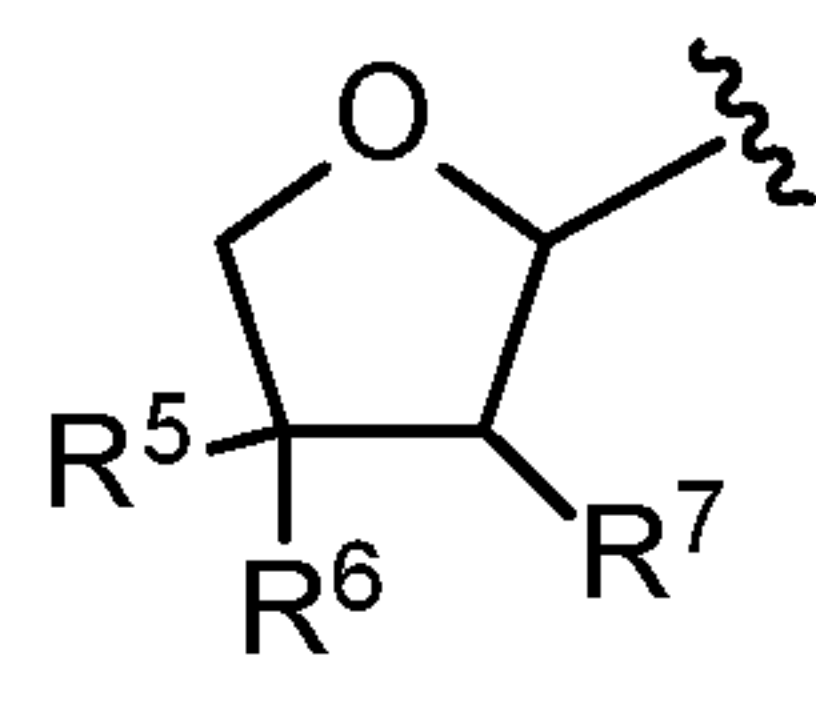


or an acceptable salt thereof, wherein R<sup>a</sup>, R<sup>b</sup>, R<sup>c</sup>, and R<sup>d</sup> are independently selected from H, OH, R, or OR;

wherein R is in each case independently selected from a hexoside of formula:



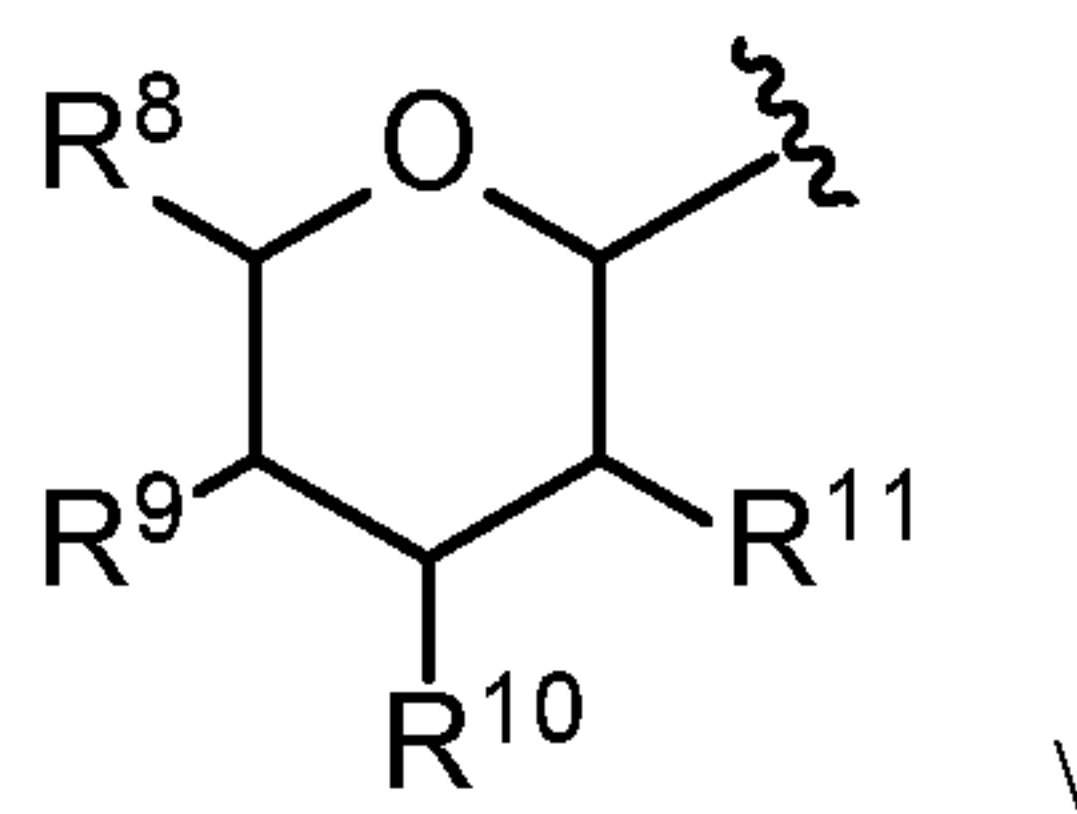
or a pentoside of formula:



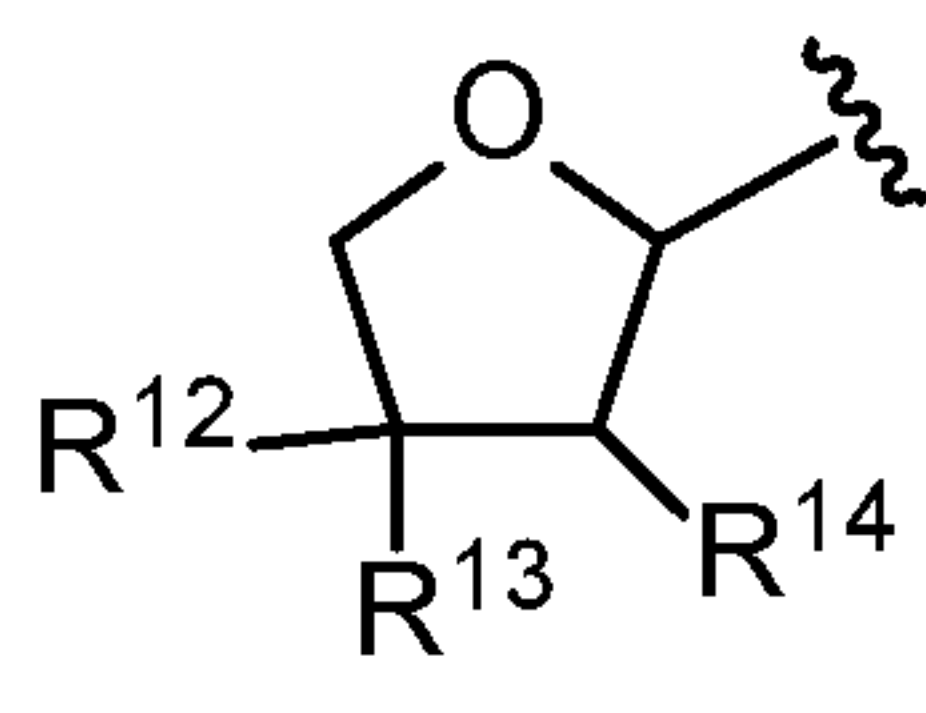
wherein  $R^1$  and  $R^5$  are independently selected from H,  $CH_3$ ,  $CH_2OH$ , or  $CH_2OR^e$ ;

$R^2$ ,  $R^3$ ,  $R^4$ ,  $R^6$ , and  $R^7$  are independently selected from H, OH, or  $OR^e$ ;

$R^e$  is a hexoside having the formula:



or a pentoside having the formula:



wherein  $R^8$  and  $R^{12}$  are selected from H,  $CH_3$  and  $CH_2OH$ ; and

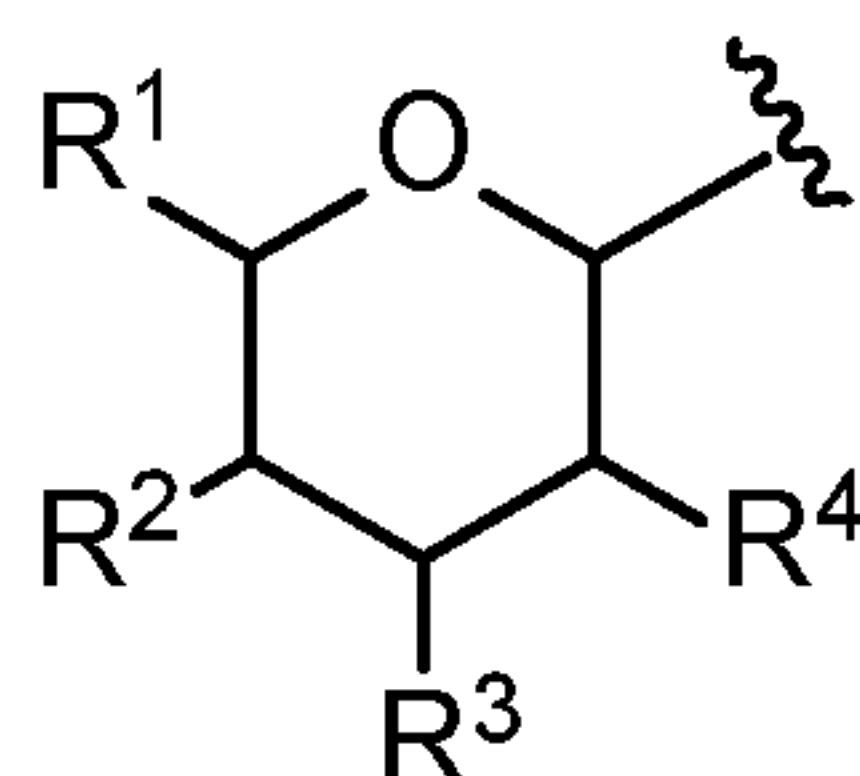
$R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{13}$ , and  $R^{14}$  are independently selected from H and OH.

16. The method according to any preceding claim, wherein at least one of  $R^a$ ,  $R^b$ ,  $R^c$ , and  $R^d$  is R or OR.

17. The method according to any preceding claim, wherein  $R^a$  and  $R^c$  are each OH, and  $R^b$  and  $R^d$  are independently selected from R and OR.

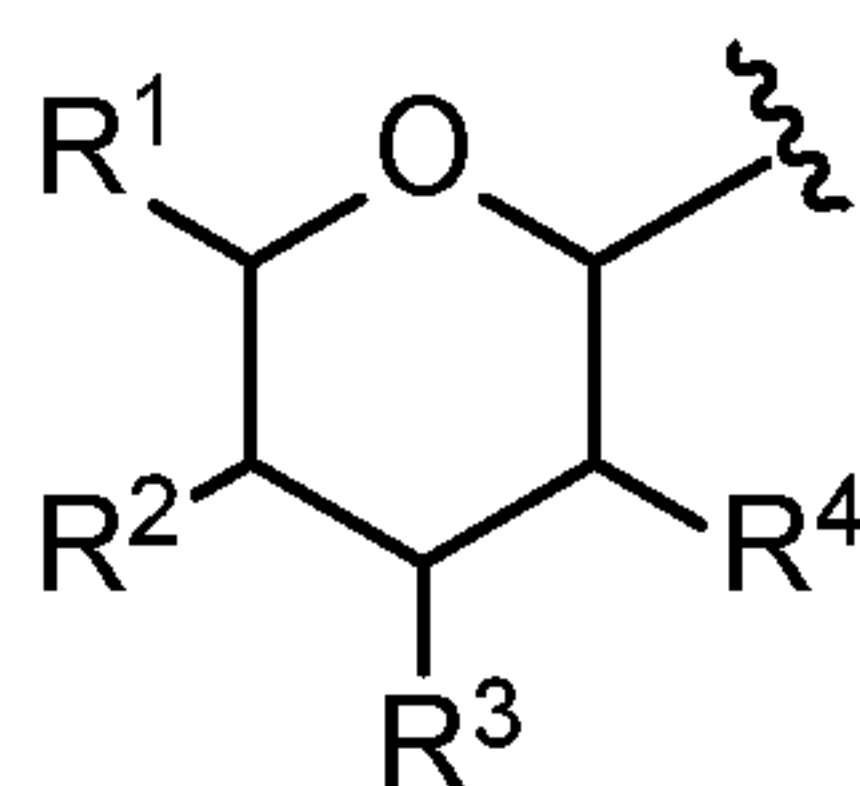
18. The method according to any preceding claim, wherein  $R^a$  and  $R^c$  are each OH, and  $R^b$  and  $R^d$  are each OR.

19. The method according to any preceding claim, wherein  $R^b$  is a hexoside having the formula:



20. The method according to claim 5, wherein for  $R^b$ ,  $R^1$  is  $CH_2OH$  and each of  $R^2$ ,  $R^3$ , and  $R^4$  are OH.

21. The method of any preceding claim, wherein  $R^d$  is a hexoside having the formula:



22. The method according to claim 7, wherein for R<sup>d</sup>, R<sup>1</sup> is H and each of R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> are OH.
23. The method according to any preceding claim, wherein the food product is a grain.
24. The method according to any preceding claim, wherein the food product is flour or dough.
25. The method according to any preceding claim, wherein the compound is added in an amount from 5-1,000 mg/kg, relative to the mass of the food product.
26. The method according to any preceding claim, wherein the flavor is modulated by reducing pinellic acid content.

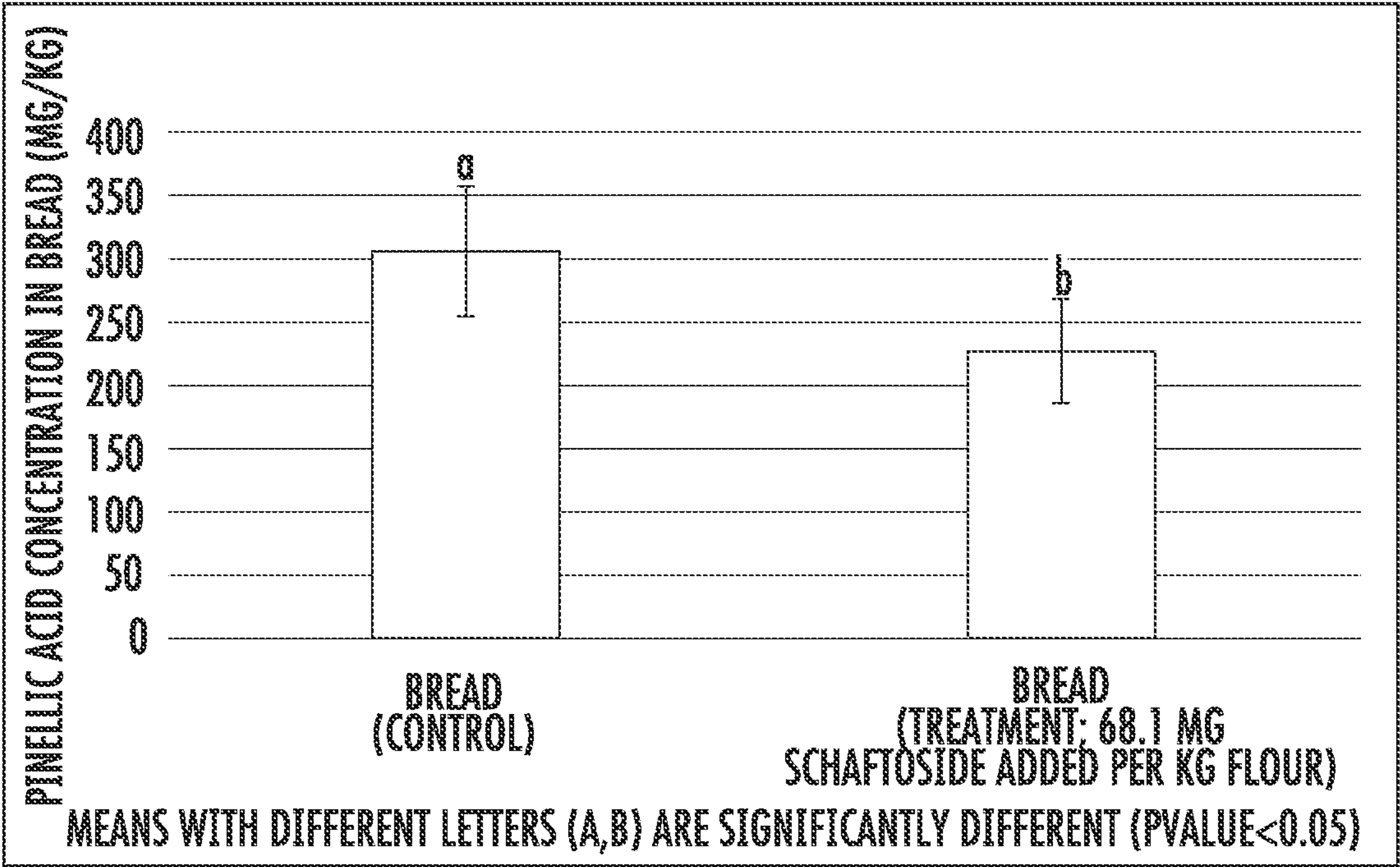


FIG. 1

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 20/57197

## A. CLASSIFICATION OF SUBJECT MATTER

IPC - A23L 2/60; A23L 27/30 (2020.01)

CPC - A23L 2/60; A23L 27/33; A23L 27/36

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)

See Search History document

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

See Search History document

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

See Search History document

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                                                                          | Relevant to claim No. |
|-----------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| A         | US 2007/0269570 A1 (DEGENHARDT et al.) 22 November 2007 (22.11.2007), especially abstract, para [0018], para [0018] table, para [0053], and para [0053] table                                                                                                                               | 1-6, 13, and 14       |
| A         | "PubChem CID 162350" Create Date: 16 September 2004 (16.09.2004), p.1 and p.2 formula                                                                                                                                                                                                       | 1-6, 13, and 14       |
| A         | "PubChem CID 5280441" Create Date: 16 September 2004 (16.09.2004), p.1 and p.2 formula                                                                                                                                                                                                      | 1-6, 13, and 14       |
| A         | GLOWACKI et al. "Determination of Total Apigenin in Herbs by Micellar Electrokinetic Chromatography with UV Detection" Journal of Analytical Methods in Chemistry vol 2016 p. 1-8 2016 (2016), especially p. 1 col 1 para 1, p. 2 col 1 Figure 1, p. 7 col 1 Table 2, and p. 7 col 1 para 1 | 1-6, 13, and 14       |
| A         | "PubChem CID 183905" Create Date: 08 September 2005 (08.09.2005), p.2 formula                                                                                                                                                                                                               | 1-6, 13, and 14       |

☐ 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

"D" document cited by the applicant in the international application

"E" earlier application or patent but published on or after the international filing date

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

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

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

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

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

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

"&amp;" document member of the same patent family

Date of the actual completion of the international search

18 December 2020 (18.12.2020)

Date of mailing of the international search report

MAR 08 2021

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents

P.O. Box 1450, Alexandria, Virginia 22313-1450

Facsimile No. 571-273-8300

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INTERNATIONAL SEARCH REPORT

International application No. .  
PCT/US 20/57197

Box No. II      Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☒ Claims Nos.: 16-19, 21 and 23-26  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III      Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
(see supplemental box)

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
claims 1-6, 13, and 14

- Remark on Protest**
- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 20/57197

## Box III: lack of unity

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I+: Claims 1-15, 20, and 22 directed to a method for modulating the flavor of a food product, comprising adding to the food product a compound having the formula depicted in claim 1 or a compound of formula (I). The compound having the formula depicted in claim 1 will be searched to the extent that the compound encompasses the first species wherein R1\* is H; R2\* is H; R3\* is H; R4\* is H; R5\* is H; R6\* is H; R7\* is H; and R8\* is H. It is believed that claims 1-6, 13, and 14 read on this first named invention, and thus these claims will be searched without fee. Applicant is invited to elect additional method(s) wherein each additional method elected will require one additional invention fee. Applicants must specify the claims that encompass any additionally elected method. Applicants must further indicate, if applicable, the claims which encompass the first named invention, if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the '+' group(s) will result in only the first claimed invention to be searched. Additionally, an exemplary election wherein different actual variables are selected is suggested. An exemplary election would be a compound having the formula depicted in claim 1 wherein R1\* is CO<sub>2</sub>H; R2\* is H; R3\* is H; R4\* is NHC(O)CH<sub>3</sub>; R5\* is CO<sub>2</sub>H; R6\* is H; R7 is H; and R8\* is NHC(O)CH<sub>3</sub> (i.e, claims 1-6 and 8-14).

The group of inventions listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

## Special Technical Features:

Group I+ includes the technical feature of a unique compound having the formula depicted in claim 1, which is not required by any other invention of Group I+.

## Common technical features:

The inventions of Groups I+ share the technical feature of a method for modulating the flavor of a food product, comprising adding to the food product a compound having the 5,7-Dihydroxy-2-(4-hydroxyphenyl)-4H-chromen-4-one core scaffold.

However, this shared technical feature does not represent a contribution over prior art, because the shared technical feature is anticipated by US 2007/0269570 A1 to DEGENHARDT et al. (hereinafter DEGENHARDT). DEGENHARDT discloses the method for modulating the flavor (para [0053]- "Example 12...taste modification") of a food product (abstract- "flavonoid sugar addition products...the use of these addition products for modifying the taste of food products" and para [0053] table, col 1 heading- "compound added to (3 mmol/L) theobromine", table col 2 heading- "% of panelists who detected a difference", and table col 3 heading- "taste/intensity"), comprising adding to the food product (para [0053] table, table col 1 heading- "compound added to (3 mmol/L) theobromine"), the compound with the 5,7-Dihydroxy-2-(4-hydroxyphenyl)-4H-chromen-4-one core scaffold (para [0053] table-last 9 rows, "2 umol/L vitexin to 222/L" to "222 umol/L isovitexin" and para [0053]- "apigenin-8-C-beta-D-glucopyranoside (vitexin)", see the document entitled "PubChem CID 5280441", p. 1- "vitexin" and p. 2 formula, and para [0053]- "apigenin-6-C-beta-D-glucopyranoside (isovitexin)", see the document entitled "PubChem CID 162350", p. 1- "isovitexin" and p. 2 formula).

As said compound was known in the art at the time of the invention, this cannot be considered a special technical feature, that would otherwise unify the inventions of Group I+.

The inventions of Groups I+ thus lack unity under PCT Rule 13.

NOTE: Claims 20 and 22 are incorrectly depending on claim 5 and 7 respectively. For the purposes of completing this ISR, claims 20 and 22 are assumed to depend on claim 15.

\*Item 4 (contd.): Claims 16-19, 21 and 23-26 are determined unsearchable because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).