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(54) NOVEL PYRAZINE FLAVORING MATERIALS

(71) We, INTERNATIONAL FLAVORS & FRAGRANCES INC., a Corporation organised under the laws of The State of New York, United States of America, of 521 West 57th Street, New York, New York, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

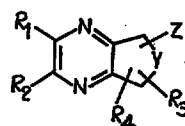
The present invention relates to certain pyrazine materials and their use in processes and compositions for altering the flavors of various materials such as tobaccos, foodstuffs, and the like, as well as the novel pyrazines and processes for producing them.

It has now been found that certain pyrazine materials are capable of imparting a wide variety of flavors to various consumable materials. Briefly, the invention contemplates altering the flavors of such consumable materials by

adding thereto a small but effective amount of at least one pyrazine material selected from any of the following classes designated I—V as described more fully hereinafter:

I. Oxycyclic Pyrazines

An oxycyclic pyrazine of the formula:



(Formula I)

wherein Y represents



Z is a carbonyl oxygen, a hydroxyl group, or an acyloxy group; and R₁, R₂, R₃, and R₄ are

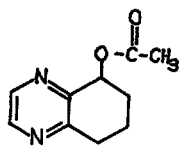
the same or different and represent hydrogen or lower alkyl having one to three carbon atoms.

- By oxycyclic pyrazines, we mean herein pyrazines to the "b" side of which are fused five- and six-membered (i.e. cyclopenta and cyclohexa) rings which are substituted with a hydroxy, acyloxy, or carbonyl oxygen atom. These rings can be substituted with one or two C_1-C_6 alkyl groups, and the pyrazine ring can also be substituted with one or two C_1-C_3 alkyl groups.

- The oxygen substituent can be a carbonyl oxygen so that the novel material is a cyclic ketone or it can be hydroxy or acyloxy. The lower acyloxy groups containing from two to four carbon atoms are desirably used herein.

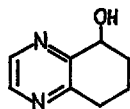
- The oxycyclic pyrazines contemplated herein include in particular those of the above formula I wherein: Y is $-CH_2-CH_2-$; Z is a carbonyl oxygen, or hydroxy, or acetyloxy; and R_1 , R_2 , R_3 and R_4 are hydrogen.

- Exemplary of the oxycyclic pyrazines contemplated herein is 5-acetoxy-5,6,7,8-tetrahydroquinoxaline having the structure



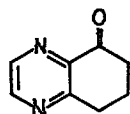
- This is a pale yellow liquid having a boiling point of 128—129°C at 0.7 mm Hg, and n_D^{25} of 1.5293, a popcorn-like odor, and a light popcorn flavor at two parts per million (ppm) in water. All parts, proportions, ratios, and percentages herein are by weight unless otherwise stated.

- Another material according to the present invention is 5-hydroxy-5,6,7,8-tetrahydroquinoxaline having the structure



- This is a white solid melting at 64.8—66.0°C having a light, nut-like odor.

- 5-Oxo-5,6,7,8-tetrahydroquinoxaline having the structure



is also contemplated. This is a yellow solid

having a roasted cereal aroma, and a melting point of 57.4°—5.98°C.

The oxycyclic pyrazines prepared according to the present invention can be obtained by a number of reaction routes. The acyloxy derivatives can be prepared by reacting a cyclohexapyrazine or a cyclopentapyrazine with a peracid in the presence of the corresponding lower (C_2-C_4) alkanolic acid and treating the reaction product with an aliphatic carboxylic acid anhydride. The peracid can be a lower (C_2-C_4) aliphatic peracid such as peracetic, perpropionic and like acids.

The aforesaid cycloalkapyrazine can be prepared by a number of reaction routes, as for example by reacting a 2-halocycloalkanone, e.g., 2-chlorocyclohexanone, or an alkyl-substituted 2-halocycloalkanone, with ethylene diamine or a 1-alkyl or a 1,2-dialkyl derivative thereof to obtain the dihydropyrazine and then dehydrogenating the pyrazine ring, as for example by passing oxygen through a solution of the pyrazine. With 2-chlorocyclohexanone and ethylene diamine, 5,6,7,8-tetrahydroquinoxaline is produced.

The quantity of peracid used is desirably at least stoichiometric with the quantity of pyrazine derivative used so as to obtain high reaction completion. Excesses of peracid up to 20 percent can be used, but quantities in excess of this are wasteful of the reactants, complicate recovery of the product, and can produce unwanted side reactions. It is accordingly desirable to utilize peracid in quantities of from stoichiometric to a 20 percent excess.

The reaction may be carried out at temperatures above 60°C to provide desirable reaction velocities. On the other hand, temperatures above 120°C can cause an overly vigorous reaction with the production of unwanted highly oxidized and other undesirable by-products. It is accordingly desirable to carry out the reaction at from 60° to 120°C. It has been found that good results can be obtained in the preferred temperature range of from 70° to 85°C.

This step of the reaction takes place readily. Generally, the minimum length of time is governed by the rate at which the peracid can be added without creating an excessive temperature rise, and in the usual process equipment this can be as little as about 15 minutes. On the other hand, an additional holding period after peracid addition has been completed will serve to provide high completeness, and an additional hour or two is generally sufficient for this purpose. Accordingly, this phase of the process is carried out for from about 15 minutes to about two hours.

An alkanolic acid may be used as a reaction vehicle and moderator to provide better control over the process. Generally, the use of lower alkanolic acids is desirable, and acids having from two to four carbon atoms are preferred.

The alkanolic acid is preferably stripped off and the product of peracid treatment is then treated with a lower alkanolic acid anhydride, that is an anhydride of an aliphatic acid having

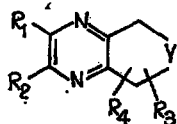
The anhydride treatment may be carried out at temperatures of from 80° to 140°C. It is preferred to carry out the reaction at the reflux temperature of the anhydride.

It is advisable for the quantity of anhydride utilized to be at least stoichiometric with the cyclic pyrazine used, and it is desirable that excesses of from 100 to 200 percent of the anhydride be used. It is advisable for the treatment with anhydride to be carried out for from about one to about six hours, and times of from one to two hours are preferred.

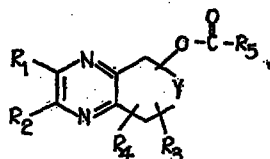
The corresponding hydroxy derivative is readily produced from the acyloxy derivative by hydrolysis with aqueous or alcoholic alkali metal hydroxide. The hydrolysis is carried out at temperatures of from about 60° to about 100°C to provide good reaction rates and completeness in from one to four hours. The hydroxides of sodium and potassium are desirably used, and methanol is a preferred alcohol.

The corresponding ketone is conveniently produced by oxidation of the alcohol. The oxidation can be carried out in a solvent or vehicle such as dimethyl sulfoxide with a lower (C₂—C₄) alkanolic anhydride such as those set forth above. The reaction is carried out at mild temperatures of from 15° to 30°C, and preferably at 20—25°C. Times of from eight to 48 hours are used, depending upon the temperature, the reactants, the vehicle, amount of agitation and the like. Jones reagent (one mole of chromium trioxide, 1/6 mole of sulfuric acid, and acetone in an amount about five times the weight of the trioxide) can also be used as an oxidizing agent in this step.

It will accordingly be apparent to those skilled in the art that a preferred route begins with the peracid oxidation of a compound having the formula



wherein R₁, R₂, R₃, R₄, Y are as set forth above, followed by treatment of the oxidation product with a lower (C₂—C₄) alkanolic acid anhydride to provide a product having the formula

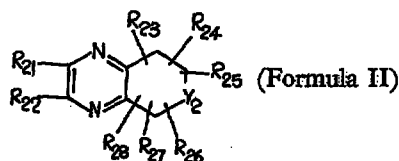


wherein R₅ is lower alkyl having one to three carbon atoms.

It will be understood by those skilled in the art that the intermediate and the final products prepared herein can be neutralized, washed, and dried to purify and cleanse the desired substances. The novel oxycyclic pyrazines can be obtained in purer form or in substantially pure form by conventional purification techniques. Thus, the products can be purified and/or isolated by distillation, extraction, preparative chromatographic techniques, and the like. It has been found desirable to purify the oxycyclic pyrazines by fractional distillation under vacuum.

II. Bicyclic Pyrazines

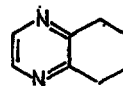
A bicyclic pyrazine having the formula



wherein Y₂ is (—CH₂—)_{n₂}; n₂ is an integer from 1 to 5, inclusive; and R₂₁, R₂₂, R₂₃, R₂₄, R₂₅, R₂₆, R₂₇, and R₂₈ are the same or different and represent hydrogen or lower alkyl having one to three carbon atoms.

More specifically, the bicyclic pyrazines according to this invention are pyrazines to the "b" side of which is fused a six- to ten-membered hydrocarbon ring. Such ring can be substituted with one or more C₁—C₃ alkyl groups, and the pyrazine ring can also be substituted with one or two C₁—C₃ alkyl groups. It will be appreciated from the present disclosure by those skilled in the art that one or more pairs of the C₁—C₃ alkyl groups substituent on the hydrocarbon ring can be geminal, i.e., can be attached to the same ring carbon atom.

A particularly preferred bicyclic pyrazine for use herein is 5,6,7,8-tetrahydroquinoxaline having the formula

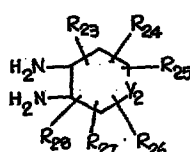


This clear to yellowish liquid has nut-like strong cereal, fried corn-like odor and flavor characteristics, as further described herein-after.

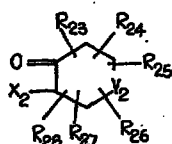
The C₁—C₃ alkyl derivatives of this material have interesting flavor and odor character and include 5 - methyl - 5,6,7,8 - tetrahydroquinoxaline, 2 - ethyl - 5,6,7,8 - tetrahydro-

quinoxaline, 2 - methyl - 7 - propyl - 5,6,7,8 - tetrahydroquinoxaline, 5,6 - diethyl - 5,6,7,8 - tetrahydroquinoxaline, 5,7 - dimethyl - 5,6,7,8 - tetrahydroquinoxaline, and the like. Thus, for example, 2,3 - dimethyl - 5,6,7,8 - tetrahydroquinoxaline is obtained according to the present invention as a colorless crystalline material having a tobacco-honey aroma. 5,7,7 - Trimethyl - 5,6,7,8 - tetrahydroquinoxaline is a liquid having a pleasant honey, tobacco flavor, while pyrazino[b]cyclodecane is a yellowish liquid having a peanut and cracker-like flavor character.

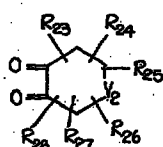
The novel bicyclic pyrazines prepared according to the present invention can be obtained by a number of reaction routes, as (i) by reacting 1,2-diaminocyclohexane or monoalkyl- or polyalkyl-substituted 1,2-diaminocyclohexane with glyoxal (a "dioxoalkane") or 1-alkyl or 1,2-dialkyl derivatives thereof, e.g., 2,3-butanedione under ring-closing conditions, or (ii) by reacting a 2-halocyclohexanone with ethylene diamine (a vicinal diaminoalkane) or a 1-alkyl or 1,2-dialkyl derivative thereof, e.g. 2,3-diaminobutane, or (iii) by reacting an aliphatic ethylenediamine or an alkyl or 1,2-dialkyl derivative thereof with a 1,2-cyclohexadione or a mono- or polyalkyl derivative thereof. The bicyclic hydropyrazine compound (or mixture of isomers thereof) obtained upon ring-closure is then dehydrogenated as necessary to provide the fused pyrazine ring. More generally, the cyclic reactant in these three reaction routes may be a compound of the respective formula shown below (X_2 being halogen):



(Route (i))



(Route (ii))



(Route (iii))

The non-cyclic reactant employed therewith may be a compound of the general formula $R_{21}-CO-CO-R_{22}$ in route (i) or $R_{21}-CHNH_2-CHNH_2-R_{22}$ in route (ii) or (iii).

Analogous compounds containing seven- to ten-membered rings fused to the pyrazine ring can thus be prepared similarly to the above-mentioned compounds containing six-membered rings but utilizing 1,2-diaminocycloheptane or mono- or polyalkyl derivatives thereof, or the analogous derivatives of cyclooctane, cyclononane or cyclodecane, instead of the diamino-cyclohexanes with the dioxoalkane, or utilizing 2-halocycloheptanone or its monoalkyl or polyalkyl derivatives, or the analogous derivatives of cyclooctane, cyclononane or cyclodecane, with ethylene diamine or its derivatives instead of 1,2 - diaminocyclohexane, or utilizing 1,2 - cycloalkadione or polyalkyl derivatives thereof with ethylene diamine or its derivatives instead of cyclohexadione. Thus, for example, either (1) a 1,2-diaminocyclohexane or -cycloheptane and the dioxo compound or (2) a 2-halo-cyclohexanone or -cycloheptanone and a vicinal diaminoalkane are admixed preferably below $10^\circ C$ to form respectively, in case (1) above the dihydropyrazino[b]cyclohexane or, the dihydropyrazino[b]cycloheptane and in case (2) above, the tetrahydropyrazino[b]cyclohexane and the tetrahydropyrazino[b]cycloheptane and double bond isomers thereof.

Examples of the 1,2-diaminocyclohexane and 1,2-diaminocycloalkanes are:

1,2-diaminocyclohexane;
1,2-diamino-4,5-dimethylcyclohexane;
1,2-diamino-3,3,5,5-tetramethylcyclohexane;
1,2-diamino-3,4,4-triethylcyclohexane;
1,2-diamino-3,3-dimethyl-4,4-diethylcyclohexane;
1,2-diaminocycloheptane;
1,2-diamino-5-methylcycloheptane;
1,2-diamino-3,3,5,5-tetramethylcycloheptane;
1,2-diamino-3,3-dimethyl-5,5-diethylcycloheptane; and
1,2-diamino-3,7-dimethylcyclodecane,

Examples of 2-halo-cycloalkanones are:

2-chlorocyclohexanone;
2-bromocyclohexanone;
2-chloro-3,4-dimethylcyclohexanone;
2-chloro-3,3,5,5-tetramethylcyclohexanone;
2-bromocycloheptanone;
2-bromo-3,4,5-triethylcycloheptanone;
2-bromo-3,4,5,6-tetramethylcycloheptanone; and
2-chloro-5-methylcyclodecanone.

Examples of the 1,2-cycloalkadiones capable of being utilized herein are:

- 1,2-cyclodecadione;
- 4,4-dimethyl-1,2-cyclodecadione;
- 5 3,7-diethyl-1,2-cyclononadione;
- 3,4,5-trimethyl-7-ethyl-1,2-cyclononadione;
- 1,2-cyclononadione;
- 1,2-cyclooctadione;
- 3-methyl-1,2-cyclohexadione;
- 10 4-methyl-1,2-cycloheptadiene; and
- 1,2-cycloheptadione.

In the case of route (i), i.e. in reactions involving dioxalkanes, the temperature of the reaction should be below the freezing point of water, and is desirably from -10°C to -80°C , to prevent decomposition of the dihydropyrazine to unwanted by-products. Temperatures below -80°C are not necessary and can require excessive time for completion of the reaction. In the case of route (ii), i.e. employing a halocycloalkanone, temperatures from -80° to $+10^{\circ}\text{C}$ should be used. In routes (i) and (ii), it is preferred to utilize temperatures of from -30°C to -15°C . In the case of route (iii), i.e. for reactions involving 1,2-cycloalkadiones, temperatures of from 50 to 100°C are utilized.

After the formation of the hydropyrazine bicyclic compound (or mixture of isomers thereof) it is dehydrogenated, as mentioned earlier, to provide the corresponding pyrazine derivative. This may be carried out at an alkaline pH obtained by adding a strong alkali metal hydroxide or an equivalent material such as an alkali metal carbonate. The hydroxides of sodium or potassium are desirably used.

The hydroxide-containing mixture may then be treated with oxygen at a temperature of from 20° to 50°C to provide a satisfactory reaction rate while minimizing undesirable side reactions and the ebullition of the reactants. The oxygen can be pure or can contain inert diluents. Air can be used as the oxygen source.

The oxygen may be added to the reactants by sparging or otherwise bubbling the gas through the reaction mixture. At the temperatures used herein, the times for the reaction may suitably range from 30 minutes to 24 hours, and it is desirable to carry out the reaction such that it attains a high degree of completion in from about one to three hours.

The reaction is desirably carried out in an inert reaction vehicle to reduce polymer formation, to permit better control over the reaction temperature, and to improve mixing of the reactants. The preferred inert reaction vehicles are solvents and include alkanols, preferably C_1 — C_8 lower alkanols such as methanol, ethanol and the like.

After the reaction is completed, as readily determined by gas chromatography, the pH of the reaction mixture can, if desired, be reduced

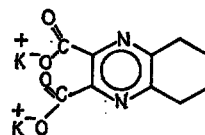
by the addition of an acid, desirably a strong mineral acid such as dilute sulfuric acid, preferably 10% to 50% sulfuric acid. If any undissolved hydroxide exists at this point then it is preferred that it be removed, as by centrifugation or filtration. The crude bicyclic pyrazine is then stripped of vehicle and further purified as desired according to the procedures hereinafter described.

The ratio of diaminocycloalkane to the glyoxal or of cycloalkadione to diaminoalkane can be stoichiometric, but better yields are frequently obtained with amounts of glyoxal or diaminoalkane in up to 10% excess of stoichiometric. It will be appreciated by those skilled in the art that use of 1,2-diamino-3-ethylcyclohexane with glyoxal will provide 5-ethyl-5,6,7,8-tetrahydroquinoxaline and reaction of 1,2-diaminocyclohexane with diacetyl will provide a 2,3-dimethyl-5,6,7,8-tetrahydroquinoxaline, and so on.

The tetrahydroquinoxaline according to the present invention can also be prepared by oxidation and subsequent acidification of 1,2,3,4-tetrahydrophenazine to form tetrahydroquinoxaline dicarboxylic acid or the alkali metal salt thereof and pyrolysis of the acid or salt to the quinoxaline.

The initial oxidation reaction may be carried out with a strong oxidizing agent such as aqueous alkali metal permanganate, desirably potassium permanganate. In order to obtain good yields without unduly long reaction times, the reaction is desirably carried out at temperatures of at least about 75°C . In aqueous solution at atmospheric pressure this reaction can be carried out at temperatures of about 100°C , although higher temperatures are possible at superatmospheric pressures. The desirable temperature range for use herein is accordingly from 75°C to 100°C , and temperatures from 80°C to 95°C are preferred.

After ring cleavage with the oxidizing agents, the manganese dioxide precipitate obtained may be filtered, centrifuged, or otherwise removed from the aqueous solution (which aqueous solution contains substantially all of the product of reaction) and washed several times with water to recover all traces of the product which has the structure:



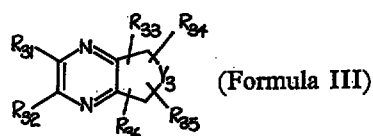
The dicarboxylate-containing solution may then be acidified with an acid, desirably a strong mineral acid such as sulfuric, hydrochloric, and the like, to precipitate the dicarboxylic acid. Hydrochloric acid is a preferred mineral acid. The acidified material may then be concentrated to remove water.

The dicarboxylic acid may be recovered by filtration and is pyrolyzed, e.g. at from 180° to 300°C, to provide the pyrazine. The pyrolysis is discontinued when the reaction is completed,

- 5 as evidenced by cessation of CO₂ evolution.
- It will be understood by those skilled in the art that the intermediate and the final products prepared herein may be neutralized, washed, and dried to obtain the desired substances. The novel bicyclic pyrazines can be obtained in purer form or in substantially pure form by conventional purification techniques. Thus, the products can be purified and/or isolated by distillation, extraction, crystallization, preparative chromatographic techniques, and the like. It has been found desirable to purify the bicyclic pyrazines by fractional distillation under vacuum.

III. Heterocyclic fused Pyrazines

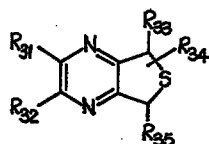
- 20 A heterocyclic fused pyrazine having the formula:



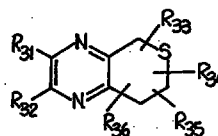
- 25 wherein Y₃ represents —O—, —S—, —CH₂—S—, or —CH₂—O—, and R₃₁, R₃₂, R₃₃, R₃₄, R₃₅, and R₃₆ are the same or different and represent hydrogen or lower alkyl having one to three carbon atoms.

- 30 More specifically, the heterocyclic fused pyrazines according to this invention are pyrazines to the "b" side of which are fused five- and six-membered oxygen- or sulfur-containing rings; these rings comprise dihydrofuran, dihydrothiophene, dihydropyran, and the sulfur analog of such pyran. Such rings can be substituted with one or more C₁—C₃ alkyl groups. The pyrazine ring can also be substituted with one or two C₁—C₃ alkyl groups, and such substituents on the heterocyclic ring can, in some cases, be geminal.

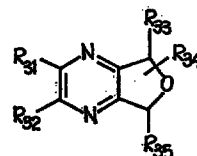
- 40 Thus, the present invention contemplates 5,7-dihydrothieno [3,4-b]pyrazines having the formula:



- 45 7,8 - dihydro - 5H - thiapyrano[3,4 - b]-pyrazines having the formula:

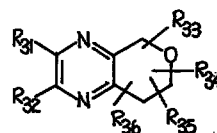


5,7 - dihydrofuro[3,4 - b]pyrazines having the formula:



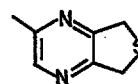
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and 7,8 - dihydro - 5H - pyrano[3,4 - b]-pyrazines having the formula:



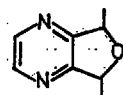
Exemplary of heterocyclic fused pyrazines prepared according to this invention is 2 - methyl - 5,7 - dihydrothieno[3,4 - b]pyrazine having the formula:

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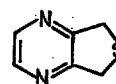
This material is a white crystalline solid having a roasted nut-like odor. Another pyrazine according to this invention is 5,7 - dihydro - 5,7 - dimethylfuro[3,4 - b] - pyrazine having the formula:

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and a roasted aroma character. A further illustrative pyrazine according to this invention is 5,7 - dihydrothieno[3,4 - b]pyrazine having the formula:

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and being a solid melting at 88—89°C with a roasted nut flavour.

The novel pyrazines prepared according to the present invention can be obtained by a number of reaction routes. The dihydrothienopyrazines can be prepared by reacting a 3,4-aminothiophane or a mono- or dialkyl substituted 3,4-diaminothiophane with an α -diketone in the presence of an alkali metal hydroxide and subsequently dehydrogenating the reaction product. The hydroxides of sodium or potassium are desirably used.

The dihydrothienopyrazines are also obtainable by reacting an alkali metal hydrosulfide with a 2,3-di(haloalkyl)pyrazine at a temperature of from 50—100°C.

In the former of these two methods of preparing dihydrothienopyrazines, the dehydrogenation of the reaction product present in the alkaline mixture first produced may be effected by treating the alkaline mixture with oxygen at a temperature of from 15° to 50°C to provide a satisfactory reaction rate while minimizing undesirable side reactions and the ebullition of the reactants. The oxygen can be pure or can contain inert diluents. It has been found desirable to use air as a source of oxygen.

The oxygen may be added to the reactants by sparging or otherwise bubbling the gas through the reaction mixture. At the temperatures used herein, the times for the reaction may suitably range from one to 24 hours, and it is desirable to carry out the reaction such that it attains a high degree of completion in from about 8 to 12 hours.

The reaction is desirably carried out in an inert reaction vehicle to permit better control over the reaction temperature and to improve mixing of the reactants. The preferred inert reaction vehicles are solvents and include alkanols, preferably C₁—C₃ alkanols such as methanol, ethanol and the like, oxygenated solvents such as ethyl ether, ethylene glycol, and the like.

After the reaction is completed, the pH of the reaction mixture may be reduced by the addition of an acid, desirably a strong mineral acid such as dilute sulfuric acid, preferably 10% to 50% sulfuric acid. The pH need not be reduced to neutrality, but it is desirable that it be reduced to or below 9, and it is generally preferred to reduce the pH to 8.0—8.5, but not lower than about 7.

The dihydrofuropyrazines are conveniently prepared by reacting a vicinal alkanedione dihalide with 1,2-diaminoethane or a mono- or dialkyl derivative thereof. Thus, a dione having the formula:



wherein each X₁ is a halogen atom and R_{3,7} and R_{4,8} are hydrogen or lower alkyl having

one to three carbon atoms can be reacted with 1,2-diaminoethane, a 1-alkyl-1,2-diaminoethane, or a 1,2-dialkyl-1,2-diaminoethane, and the resulting intermediate product oxidized to obtain the furopyrazine. The two X₂ atoms are desirably both Cl or both Br, and are preferably both Br.

As taught above, a 1,2-diaminoethane is utilized, except that when the pyrazine ring of the heterocyclic fused pyrazine produced is to be mono- or dialkyl-substituted the diaminoethane can be 1-alkyl- or 1,2-dialkyl-substituted.

The reaction may be carried out at low temperatures not substantially above 0°C, and temperatures down to -40°C are preferably utilized. At temperatures above 0°C the reaction proceeds too vigorously, is difficult to control, and provides unwanted by-products, while at temperatures below -40°C the reaction rate becomes very sluggish. It is accordingly desirable to utilize temperatures of from 0°C to -40°C. Temperatures of from about -5°C to about -20°C are particularly preferred.

After this first step of the reaction is completed, the mixture is oxidized to produce the dihydrofuran ring. The oxidation may be carried out at an alkaline pH, desirably in the presence of an alcoholic alkali metal hydroxide. Preferred alcohols are the C₁—C₃ alkanols, particularly methanol and ethanol. Preferred hydroxides are sodium and potassium.

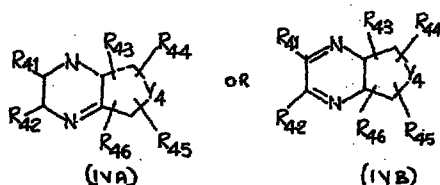
The temperature of the oxidizing reaction can range from 20°C to 50°C. At higher temperatures the rings can be oxidized, and at lower temperatures the reaction proceeds with a very low velocity.

The thiapyranopyrazines are prepared by reacting 1,2-diaminoethane or 1-alkyl or 1,2-dialkyl derivatives thereof with 3-chlorothiopyran-4-one or alkyl-substituted derivatives thereof, desirably at the low temperatures described herein. The pyrans are similarly prepared from the reaction of such diamines with 3-chloropyrones or alkyl-substituted derivatives thereof. The pyrazine is produced from the reaction products by oxidation in the presence of alkalis as described above.

It will be understood by those skilled in the art that the intermediate and the final products prepared herein can be neutralized, washed, and dried to obtain the desired substances. The novel cyclic pyrazines can be obtained in purer form or in substantially pure form by conventional purification techniques. Thus, the products can be purified and/or isolated by distillation, extraction, crystallization, preparative chromatographic techniques, and the like. It has been found desirable to purify the heterocyclic fused pyrazines by fractional distillation under vacuum.

IV. Bicyclic Dehydropiperazines

A bicyclic dehydropiperazine having the formula:



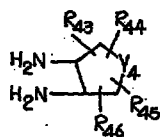
5 (Formula IVA) (Formula IVB)

wherein Y_4 is $(-CH_2-)_n$; n is an integer from one to six, inclusive; one dashed line represents a double bond and the other represents a single bond; and R_{41} , R_{42} , R_{43} , R_{44} , R_{45} and R_{46} are the same or different and represent hydrogen or lower alkyl having one to three carbon atoms.

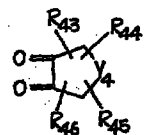
More specifically, the bicyclic dehydropiperazines according to this invention are partially reduced pyrazines with a five- to ten-membered hydrocarbon ring fused to the "b" side of the reduced pyrazine ring. Such hydrocarbon ring can be substituted with one or more C_1-C_3 alkyl groups, and the diazine ring can also be substituted with one or two C_1-C_3 alkyl groups. It will be appreciated from the present disclosure by those skilled in the art that one or more pairs of the C_1-C_3 alkyl groups substituent on the carbocyclic ring can be geminal, i.e., can be attached to the same ring carbon atom.

A bicyclic dehydropiperazine having the formula IVA or IVB can be prepared from a diaminocycloalkane of the following general formula (a) or from a 1,2-cycloalkadione of the following general formula (b):

(a):



(b):

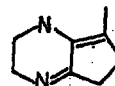


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Compound (a) is reacted with a dioxoalkane having the formula $R_{41}-CO-CO-R_{42}$ at a temperature of from $-80^\circ C$ to $50^\circ C$, and compound (b) with a diaminoalkane having the

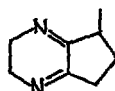
formula $NH_2-CHR_{41}-CHR_{42}-NH_2$ at a temperature of from 50° to $150^\circ C$, to produce a bicyclic dehydropiperazine compound (R_{41} , R_{42} , R_{43} , R_{44} , R_{45} and R_{46} are as defined above).

A particularly preferred bicyclic piperazine for use herein is 5 - methyl - 3,4,6,7 - tetrahydro - 2(H) - cyclopentapyrazine having the structure

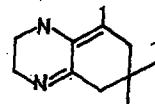


This is a crystalline solid having a melting point of $117-121^\circ C$. It has a roasted nut, burnt aroma.

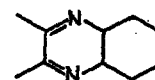
Another material according to the present invention is 5 - methyl - 3,5,6,7 - tetrahydro - 2(H) - cyclopentapyrazine having the structure



Another material exemplifying the present invention is 5,7,7 - trimethyl - 2,3,4,6,7,8 - hexahydroquinoxaline having the formula

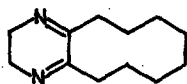


This material has a sweet, tobacco-like fragrance note. It is a pale, yellow solid. The invention is further exemplified by 2,3 - dimethyl - 4a,5,6,7,8,8a - hexahydroquinoxaline having the formula



This material has an interesting tobacco-like, buttery aroma character and is a white solid which turns tan and finally blue after storage. Both cis and trans isomers are encompassed within the the above formula, and the melting point of the material varies over a range depending upon the ratio of the cis-trans ring junction isomers encompassed in the foregoing formula.

A further bicyclic dehydropiperazine according to the invention is 2,3,5,6,7,8,9,10,11,12 - decahydrocyclodecapyrazine having the formula



As indicated earlier, the novel bicyclic dehydropiperazines prepared according to the present invention can be obtained by reacting a diaminocycloalkane or monoalkyl- or polyalkane-substituted diaminocycloalkane with a "dioxoalkane" (glyoxal or 1-alkyl or 1,2-dialkyl derivatives thereof, e.g., 2,3-butandione), or by reacting ethylenediamine or an alkyl or 1,2-dialkyl derivative thereof with a 1,2-cycloalkadione or a mono- or polyalkyl derivative thereof.

Examples of the 1,2-diaminocycloalkanes are as follows:

- 1,2-diaminocyclohexane;
- 1,2-diamino-4,5-dimethylcyclohexane;
- 1,2-diamino-3,4,5,5-tetramethylcyclohexane;
- 1,2-diamino-3,4,4-triethylcyclohexane;
- 1,2-diamino-3,3-dimethyl-5,5-diethylcyclohexane;
- 1,2-diamino-3-methylcyclooctane;
- 1,2-diaminocyclodecane;
- 1,2-diaminocyclopentane;
- 1,2-diaminocycloheptane;
- 1,2-diamino-5-methylcycloheptane;
- 1,2-diamino-4,4,5,6-tetramethylcyclohexane; and
- 1,2-diamino-3,3-dimethyl-4,4-diethylcycloheptane.

Examples of the 1,2-cycloalkadiones capable of being utilized herein as follows:

- 3-methyl-1,2-cyclohexadione;
- 1,2-cycloheptadione;
- 1,2-cyclohexadione;
- 3-methyl-1,2-cyclohexadione;
- 1,2-cyclopentadione;
- 1,2-cyclodecadione;
- 3-methyl-1,2-cyclopentadione;
- 4,5-dimethyl-1,2-cyclopentadione;
- 3-ethyl-1,2-cyclopentadione;
- 3-ethyl-1,2-cyclohexadione;
- 3-propyl-1,2-cyclohexadione;
- 3-ethyl-4-propyl-1,2-cyclohexadione;
- 4-methyl-1,2-cyclooctadione;
- 4-methyl-1,2-cyclodecadione;
- 4-methyl-1,2-cyclononadione; and
- 5-propyl-1,2-cyclodecadione.

It will be understood that the enolic form of the alkadione can also be utilized and that the alkadione will be taken to include the enol form.

In reactions involving dioxoalkanes, the temperature of the reaction is kept below 50°C to

prevent decomposition of the dehydropiperazine to unwanted by-products. Temperatures below -80°C require excessive time for completion of the reaction. It is accordingly appropriate to use the above-mentioned temperatures from -80°C to 50°C, and it is preferred to utilize temperatures of from -30°C to 25°C. For reactions involving 1,2-cycloalkadiones, vehicle reflux temperatures are utilized, these being from 50° to 150°C.

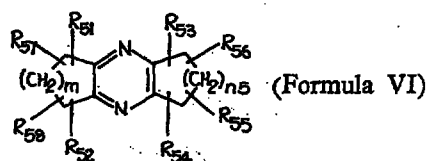
The reaction is desirably carried out in an inert reaction vehicle to reduce polymer formation, to permit better control over the reaction temperature, and to improve mixing of the reactants. The preferred inert reaction vehicles are solvents and include alkanols, preferably C₁-C₃ alkanols such as methanol, and aryl hydrocarbons such as benzene, toluene, xylene, and the like. The crude bicyclic dehydropiperazine is then stripped of vehicle and further purified as desired according to the procedures hereinafter described.

The ratio of diaminocycloalkane to the glyoxal, or of cycloalkadione to diaminoalkane, can be stoichiometric, but better yields are frequently obtained with amounts of dioxoalkane, such as glyoxal or diaminoalkane in excess of stoichiometric. It is accordingly desirable to utilize quantities of the dioxoalkane or diaminoalkane up to a threefold excess of stoichiometric. It will be appreciated by those skilled in the art that use of 1,2 - diamino - 3 - ethylcyclohexane with glyoxal yields 5 - ethyl - 4a,5,6,7,8,8a - hexahydroquinoxaline and reaction of 1,2-diaminocyclohexane with diacetyl will provide 2,3 - dimethyl - 4a,5,6,7,8,8a - hexahydroquinoxaline, and so on.

It will be understood according to the present invention that the products prepared herein can be neutralized and purified to yield the desired substances. The novel bicyclic dehydropiperazines can be obtained in purer form or in substantially pure form by conventional purification techniques. Thus, the products can be purified and/or isolated by distillation, sublimation, extraction, crystallization, preparative chromatographic techniques, and the like.

V. Tricyclic Pyrazines

A tricyclic pyrazine having the formula

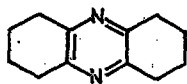


wherein m and n are each an integer from 1 to 6, inclusive; and R_{51} , R_{52} , R_{53} , R_{54} , R_{55} , R_{56} , R_{57} , and R_{58} are the same or different

and represent hydrogen or lower alkyl having one to three carbon atoms.

More specifically, the tricyclic pyrazines used according to this invention are pyrazines to the "b" and "e" sides of which are fused five- to ten-membered hydrocarbon rings. Such rings can be substituted with one or more C_1-C_3 alkyl groups. It will be appreciated from the present disclosure by those skilled in the art that one or more pairs of the C_1-C_3 alkyl groups substituent on the hydrocarbon ring can be geminal, i.e., can be attached to the same ring carbon atom.

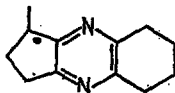
A tricyclic pyrazine for use herein is 1,2,3,4,6,7,8,9 - octahydrophenazine having the formula



This yellowish viscous liquid has fried corn chip odor and flavor characteristics, as further described hereinafter.

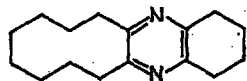
Another tricyclic pyrazine according to this invention is 1 - methyl - 2,3,5,6,7,8 - hexahydro - 1(H) - cyclopenta[b]quinoxaline having the formula

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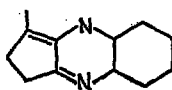
This substance is a pale yellowish liquid having a nut-like aroma.

A further tricyclic pyrazine used herein is the novel material 1,2,3,4,6,7,8,9,10,11,12,13-dodecahydrocycloclodeca[b]quinoxaline having the formula

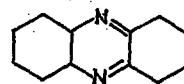


This oily material has a light, sweet nut flavor and aroma character.

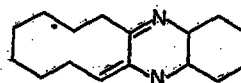
The following intermediates are particularly useful in the preparation of the various tricyclic pyrazines:



1 - methyl - 3,4a,5,6,7,8,8a,9 - octahydro - 2(H) - cyclopenta[b]quinoxaline;

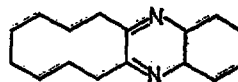


1,2,3,4,4a,6,7,8,9,10a-decahydrophenazine;

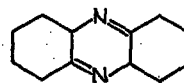


1,2,3,4,4a,5,7,8,9,10,11,12,13,14a - tetradecahydrocycloclodeca[b]quinoxaline;

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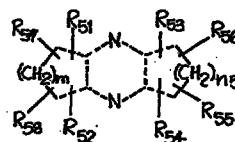


1,2,3,4,4a,6,7,8,9,10,11,12,13,14a - tetradecahydrocycloclodeca[b]quinoxaline; and
1,2,3,4,4a,6,7,8,9,9a - decahydrophenazine:



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It will accordingly be appreciated that the present invention also provides novel asymmetric tricyclic pyrazines having the formula



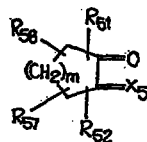
wherein m and n_s are different integers from one to six, inclusive; two or three of the dashed lines represent non-allenic double bonds, of which not more than one is outside the N-containing ring; and R_{51} , R_{52} , R_{53} , R_{54} , R_{55} , R_{56} , R_{57} , and R_{58} are hydrogen or lower alkyl having from one to three carbon atoms. Preferred tricyclic pyrazines of this latter formula are those wherein there are three double bonds in the heterocyclic ring; m is one; n_s is two; R_{51} is a methyl substituent on a carbon atom adjacent to the heterocyclic ring; and R_{52} , R_{53} , R_{54} , R_{55} , R_{56} , R_{57} and R_{58} are hydrogen.

The tricyclic pyrazines prepared according to the present invention can be obtained by a number of reaction routes, as by reacting a 1,2-diaminocycloalkane or monoalkyl- or polyalkyl-substituted 1,2-diaminocycloalkane with

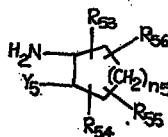
a 1,2-cycloalkanedione or monoalkyl- or polyalkyl-substituted derivatives thereof under ring-closing conditions or by reacting such 1,2-diaminocycloalkanes or derivatives with a 1,2-cycloalkane dione or monoalkyl- or polyalkyl-substituted derivatives thereof, followed by aromatization of the heterocyclic ring, or with a 2-halocycloalkanone or monoalkyl- or polyalkyl-substituted derivatives thereof; or by reacting a 2-aminocycloalkanone or monoalkyl- or polyalkyl-substituted derivatives thereof with a like or a different 2-aminocycloalkanone. The reactants are preferably utilized in stoichiometric proportions. The tricyclic dihydropyrazine compounds obtained upon ring-closure are then dehydrogenated as desired to provide the fused pyrazine ring.

It will accordingly be appreciated by those skilled in the art that when 1,2-diaminocyclopentane and 1,2-cyclopentanedione are reacted, m and n in the generic formula will both be one, while when 1,2-cyclodecadione and 1,2-diaminocyclopentane are reacted m will be six and n will be one. Similar results will follow from the other reactions set forth above utilizing reactants having from five to ten carbon atoms in each ring.

The reaction can accordingly be represented as one between a cyclic ketone having the formula



and a cyclic amine having the formula



wherein m and n are as set forth above; X_5 is an amino group, a halo atom, preferably bromo or chloro, or a carbonyl oxygen; and Y_5 is an amino group or a carbonyl oxygen; except that X_5 and Y_5 cannot both be amino or both be carbonyl oxygen and X_5 cannot be a halo atom when Y_5 is carbonyl oxygen; and wherein R_{51} , R_{52} , R_{53} , R_{54} , R_{55} , R_{56} , R_{57} , and R_{58} are the same or different and are hydrogen or C_1-C_8 alkyl. Thus, X_5 and

Y_5 taken together comprise one of the following pairs of groups:

X_5	Y_5	
(1) carbonyl oxygen	amino	
(2) halo atom	amino	
(3) amino	halo atom	50
(4) amino	carbonyl oxygen	

Examples of the 1,2-diaminocycloalkanes which can be used herein are:

1,2-diaminocyclopentane	
1,2-diaminocyclohexane;	55
1,2-diamino-4,5-dimethylcyclohexane;	
1,2-diamino-3,3,5,5-tetramethylcyclohexane;	
1,2-diamino-3,4,4-triethylcyclohexane;	
1,2-diamino-3,3-dimethyl-4,4-diethylcyclohexane;	60
1,2-diaminocycloheptane;	
1,2-diamino-5-methylcycloheptane;	
1,2-diamino-3,3,5,5-tetramethylcyclohexane;	65
1,2-diamino-3,3-dimethyl-5,5-diethylcycloheptane;	
1,2-diamino-3,7-dimethylcyclodecane; and	
1,2-diamino-3-methylcyclopentane.	

Examples of the 2-halo-cycloalkanones are:

2-chlorocyclohexanone;	
2-bromocyclohexanone;	
2-chloro-3,4-dimethylcyclohexanone;	
2-chloro-3,3,5,5-tetramethylcyclohexanone;	75
2-bromocycloheptanone;	
2-bromo-3,4,5-triethylcycloheptanone;	
2-bromo-3,4,5,6-tetramethylcycloheptanone;	
and	
2-chloro-5-methylcyclodecanone	80

Examples of the 1,2-cycloalkadiones capable of being utilized herein are:

3-methyl-1,2-cyclopentadione;	
1,2-cyclodecadione;	
4,4-dimethyl-1,2-cyclodecadione;	85
3,7-diethyl-1,2-cyclononadione;	
3,4,5-trimethyl-7-ethyl-1,2-cyclononadione;	
1,2-cyclononadione;	
1,2-cyclooctadione;	
3-methyl-1,2-cyclohexadione;	90
4-methyl-1,2-cycloheptadione;	
1,2-cycloheptadione; and	
1,2-cyclopentadione.	

Examples of amino cycloalkanones capable of being utilized herein are:

- 2-aminocyclopentanone-1;
- 2-aminocyclohexanone-1;
- 5 2-aminocycloheptanone-1;
- 2-aminocyclooctanone-1;
- 2-aminocyclodecanone-1;
- 2-amino-4-methylcyclononanone-1;
- 2-amino-3,3-dimethylcyclopentanone-1;
- 10 and
- 2-amino-3-methyl-4-ethylcyclohexanone-1.

The reaction of the diamine and diketone may be carried out at a temperature of from 0°C. At temperatures lower than 0°C, the reaction rate is relatively slow, while at temperatures higher than about 100°C, the reactants tend to polymerize. It is preferred to carry the reaction out at temperatures of from 70°C to 85°C. The time for the reaction to form the tricyclic pyrazine is preferably from one hour up to eight hours. It is particularly desirable to conduct the reaction so that the time required is from two to four hours.

In order to promote a more uniform reaction by moderating the rate and providing good mixing and to facilitate removal by azeotropic distillation of the water formed in the reaction, it is desirable in some aspects of the invention to utilize a liquid reaction vehicle. The vehicle is desirably a solvent for the reactants and any other ingredients which are present in the reaction mixture and forms an azeotrope with water. The vehicle can also be chosen so that the reflux temperature of the reaction mixture is within the temperature ranges as hereinbefore set forth. Thus, the preferred reaction vehicles utilized at reaction temperatures above 15°C include aromatic hydrocarbons such as benzene, toluene, xylene, and the like. Vehicles which can be utilized at lower reaction temperatures of 0° to 10°—15°C include aliphatic alcohols such as methanol, ethanol, isopropanol, and the like and aliphatic and alicyclic ethers such as tetrahydrofuran, diethyl ether, and the like. It will be understood that the alcohols can also be used at temperatures of 15°C and above.

The reaction is desirably carried out in the presence of a catalyst to promote the ring-closing reaction and form the reduced pyrazine ring. The catalysts are generally acid substances, particularly aryl sulfonic acids such as paratoluene sulfonic acid and the like. Based upon the quantity of reactants, it is desirable to use from 0.5 to five percent of such catalysts. All parts, proportions, percentages, and ratios herein are by weight unless otherwise indicated.

After the formation of the reduced tricyclic pyrazine, it is oxidized, if desired, to provide the corresponding pyrazine derivative. This is carried out at an alkaline pH obtained by adding a strong alkali metal hydroxide or an

equivalent material such as alkali metal carbonate. The hydroxides of sodium or potassium are desirably used.

The hydroxide-containing mixture may then be treated with oxygen at a temperature of from 30° to 70°C to provide a satisfactory reaction rate while minimizing undesirable side reactions and the ebullition of the reactants. The oxygen can be pure or can contain inert diluents. Air can be used as the oxygen source.

The oxygen is added to the reactants by sparging or otherwise bubbling the gas through the reaction mixture. At the temperatures used herein, the times for the reaction range from 30 minutes to 24 hours, and it is desirable to carry out the reaction so that it attains a high degree of completion in from one to five hours.

The oxidation reaction is desirably carried out in an inert reaction vehicle to reduce polymer formation, to permit better control over the reaction temperature, and to improve mixing of the reactants. The preferred inert reaction vehicles are solvents and include alkanols, preferably lower alkanols such as methanol, ethanol and the like.

After the reaction is complete, as readily determined by gas chromatography, the pH of the reaction mixture can, if desired, be reduced by the addition of an acid, desirably a strong mineral acid such as dilute sulfuric acid, preferably 10% to 50% sulfuric acid. If any undissolved hydroxide exists at this point then it is preferred that it be removed, as by centrifugation or filtration. The crude tricyclic pyrazine is then stripped of vehicle and further purified as desired according to the procedures hereinafter described.

It will be understood by those skilled in the art that the intermediate and the final products prepared herein are washed and dried to obtain the desired substances. The novel tricyclic pyrazines can be obtained in purer form or in substantially pure form by conventional purification techniques. Thus, the products can be purified and/or isolated by distillation, extraction, crystallization, preparative chromatographic techniques, and the like. It has been found desirable to purify the tricyclic pyrazines by fractional distillation under vacuum.

It will be appreciated from the present invention that the various pyrazines and mixtures thereof according to the present invention can be used to alter, vary, fortify, modify, enhance, or otherwise improve the flavor of a wide variety of materials which are ingested, consumed, or otherwise organoleptically sensed.

The term "alter" in its various forms will be understood herein to mean the supplying or imparting a flavor character or note to an otherwise bland, relatively tasteless substance, or augmenting an existing flavor characteristic where the natural flavor is deficient in some regard, or supplementing the existing flavor

impression to modify organoleptic character.

These pyrazine materials are accordingly useful in flavoring compositions. A flavoring composition is taken to mean one which contributes a part of the overall flavor impression by supplementing or fortifying a natural or artificial flavor in a material as well as one which supplies substantially all the flavor and/or aroma character to a consumable article.

The term "foodstuff" as used herein includes both solid and liquid ingestible materials for man or animals, which materials usually do, but need not, have nutritional value. Thus, foodstuffs includes meats, gravies, soups, convenience foods, malt, alcoholic, and other beverages, milk and dairy products, seafoods including fish, crustaceans, molluscs, and the like, candies, vegetables, cereals, soft drinks, snacks, dog and cat foods, other veterinary products, and the like.

The term "tobacco" will be understood herein to mean natural products such as, for example, burley, Turkish tobacco, Maryland tobacco, flue-cured tobacco and the like including tobacco-like or tobacco-based products such as reconstituted or homogenized leaf and the like, as well as tobacco substitutes intended to replace natural tobacco, such as lettuce and cabbage leaves and the like. The tobaccos and tobacco products include those designed or used for smoking such as in cigarette, cigar, and pipe tobacco, as well as products such as snuff, chewing tobacco, and the like.

When the pyrazine materials of this invention are used in a flavoring composition, they can be combined with conventional flavoring materials or adjuvants. Such co-ingredients or flavoring adjuvants are well known in the art for such use and have been extensively described in the literature. Apart from the requirement that any such adjuvant material be ingestibly acceptable, and thus non-toxic or otherwise non-deleterious, conventional materials can be used and broadly include other flavor materials, vehicles, stabilizers, thickeners, surface active agents, conditioners, and flavor intensifiers.

Such conventional flavoring materials include saturated, unsaturated, and amino acids; alcohols, including primary and secondary alcohols; esters; carbonyl compounds including ketones and aldehydes; lactones; other cyclic organic materials including benzene derivatives, alicyclics, heterocyclics such as furans, pyridines, other pyrazines and the like; sulfur-containing materials including thiols, sulfides, disulfides and the like; proteins; lipids; carbohydrates; so-called flavor potentiators such as monosodium glutamate, guanilates, and inosinates; natural flavoring materials such as cocoa, vanilla, and caramel; essential oils and extracts such as anise oil; clove oil, and the like; artificial flavoring materials such as vanillin; and the like.

Stabilizers include preservatives such as

sodium chloride, and the like, antioxidants such as calcium and sodium ascorbate, ascorbic acid, butylated hydroxyanisole, butylated hydroxytoluene, propyl gallate and the like, sequestrants such as citric acid, EDTA, phosphates, and the like.

Thickeners include carriers, binders, protective colloids, suspending agents, emulsifiers and the like, such as agar-agar, carrageenan, cellulose and cellulose derivatives such as carboxymethyl cellulose and methyl cellulose, natural and synthetic gum such as gum arabic, gum tragacanth, and the like, and other proteinaceous materials, lipids, carbohydrates, starches, and pectins.

Surface active agents include emulsifying agents such as mono- and/or diglycerides of fatty acids such as capric acid, caprylic acid, palmitic acid, myristic acid, stearic acid, oleic acid, and the like, lecithin, defoaming and flavor-dispersing agents such as sorbitan monostearate, potassium stearate, hydrogenated tallow alcohol, and the like.

Conditioners include compounds such as bleaching and maturing agents such as benzoyl peroxide, calcium peroxide, hydrogen peroxide and the like; starch modifiers such as peracetic acid, sodium chlorite, sodium hypochlorite, propylene oxide, succinic anhydride and the like, buffers and neutralizing agents such as sodium acetate, ammonium bicarbonate, ammonium phosphate, citric acid, lactic acid, vinegar and the like; colorants such as carminic acid, cochineal, turmeric, curcumin and the like; firming agents such as aluminum sodium sulfate, calcium chloride and calcium gluconate, texturizers; anti-caking agents such as aluminum calcium sulfate and tribasic calcium phosphate; enzymes; yeast foods such as calcium lactate and calcium sulfate; nutrient supplements such as iron salts such as ferric pyrophosphate, ferrous gluconate and the like, riboflavin, vitamins, zinc sources such as zinc chloride, zinc sulphate, and the like.

The pyrazines, or the compositions incorporating them, as mentioned above, can be combined with one or more vehicles or carriers for adding them to the particular product. Vehicles can be edible or otherwise suitable materials such as ethyl alcohol, propylene glycol, water, and the like. Carriers include materials such as gum arabic, carrageenan, other gums, and the like. The tricyclic pyrazines can be incorporated with the carriers by conventional means such as spray-drying, drum-drying, and the like. Such carriers can also include materials for coacervating the pyrazines (and other flavoring ingredients, as present) to provide encapsulated products. When the carrier is an emulsion, the flavoring composition can also contain emulsifiers such as mono- and diglycerides of fatty acids and the like. With these carriers or vehicles the desired physical form of the composition can

be prepared.

It will be understood by those skilled in the art that the pyrazines can be added during production of the finished product. Thus, when the pyrazines are used to alter or otherwise vary the flavor of a foodstuff, they can be added in the original mixture, dough, emulsion, batter, or the like prior to any cooking or heating operation. Alternatively, they can be added at a later stage of processing if volatilization losses would be excessive during the earlier processing.

When the materials are used to treat tobacco products, for example, the additive can be applied in a suitable manner, as by spraying, dipping, or otherwise. The pyrazines can be applied during the "casing" or final spray treatment of the tobacco, or they can be applied at some earlier stage of curing or preparation. The quantity of pyrazines or mixtures thereof utilized should be sufficient to impart the desired flavor characteristic to the product, but on the other hand, the use of an excessive amount of the pyrazines is not only wasteful and uneconomical but in some instances too large a quantity may unbalance the flavor or other organoleptic property of the product consumed. The quantity used will vary depending upon the ultimate foodstuff, tobacco product, or other consumable product; the amount and type of flavor initially present in the product; the further process or treatment steps to which the product will be subjected; regional and other preference factors; the type of storage, if any, to which the product will be subjected; and the pre-consumption treatment, such as baking, frying, and so on, given to the product by the ultimate consumer. Accordingly, the terminology "effective amount" and "sufficient amount" is understood in the context of the present invention to be quantitatively adequate to alter the flavor of the foodstuff, tobacco, or other consumable material.

It is preferred that the ultimate compositions contain from 0.005 part per million (ppm) to 100 ppm of tricyclic pyrazines. More particularly, in food compositions it is desirable to use from 0.01 to 50 ppm and in certain preferred embodiments of the invention, from 1 to 15 ppm of the pyrazines are included in the finished product. On the other hand, tobacco compositions can contain as little as 0.1 ppm and as much as 100 ppm, depending upon whether a cigarette tobacco, a pipe tobacco, a cigar tobacco, a chewing tobacco, or snuff is being prepared. All parts, proportions, percentages, and ratios herein are by weight unless otherwise indicated.

The amount of pyrazine to be utilized in the flavoring composition can be varied over a wide range depending upon a particular quality to be added to the foodstuff, tobacco, or other consumable material and the particular pyrazine employed. Thus, amounts of one or more pyrazines according to the present invention

from about 0.1 percent up to 80 or 90 percent can be incorporated in such compositions. It is generally found to be desirable to include from 0.5 to 25% of the pyrazine in such compositions.

The pyrazines of this invention are also useful individually or in admixtures as fragrances. They can be used to contribute an aroma note simulating its flavor character. As olfactory agents the pyrazines of this invention can be formulated into or used as components of a "perfume composition."

The term "perfume composition" is used herein to mean a mixture of organic compounds, including, for example, alcohols, aldehydes, ketones, nitriles, esters, and frequently hydrocarbons which are admixed so that the combined odors of the individual components produce a pleasant or desired fragrance.

In perfume compositions the individual component will contribute its particular olfactory characteristics, but the overall effect of the perfume composition will be the sum of the effect of each ingredient. Thus, the individual compounds of this invention, or mixtures thereof, can be used to alter, modify, enhance, or supplement the aroma characteristics of a perfume composition, for example, by highlighting or moderating the olfactory reaction contributed by another ingredient in the composition.

The amount of the compounds of this invention which will be effective in perfume compositions depends on many factors, including the other ingredients, their amounts, and the effects which are desired. It has been found that perfume compositions containing as little as 2% of the pyrazines of this invention, or even less, can be used to impart a scent to or alter the scent of soaps, cosmetics, and the other products. The amount employed can range up to 50% or higher and will depend on considerations of cost, nature of the end product, the effect desired on the finished product and particular fragrance sought.

The pyrazines of this invention can be used alone or in a perfume composition as an olfactory component in detergents and soaps; space odorants and deodorants; perfumes; colognes; toilet waters; bath preparations such as bath oil and bath salts; hair preparations such as lacquers, brilliantines, pomades, and shampoos; cosmetic preparations such as creams, deodorants, hand lotions, and sun screens; powders such as talcs, dusting powders, face powder, and the like. When used as an olfactory component of a perfumed article, as little as 0.01% of one or more of the pyrazines will suffice to impart its characteristic odor. Generally, no more than 0.3 percent is required.

In addition, the perfume composition can contain a vehicle or carrier for the pyrazines alone or with other ingredients. The vehicle can be a liquid such as alcohol, glycol, or the

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like. The carrier can be an absorbent solid such as a gum or components for encapsulating the composition.

- 5 The following examples are given to illustrate embodiments of the invention as it is presently preferred to practice it. It will be understood that these examples are illustrative, and the invention is not to be considered as restricted thereto except as indicated in the
10 appended claims.

Examples

I. Preparation and Utilization of Oxycyclic Pyrazines:

Preparation of 5-Acetoxy-5,6,7,8-tetrahydroquinoxaline

- 15 A one-liter reaction flask fitted with an agitator, thermometer, reflux condenser and addition funnel is charged with 200 cc of acetic acid, and 53.6 g (0.4 mole) of 5,6,7,8-tetrahydroquinoxaline is added. The mixture is brought to 75°C and 76.0 g (0.4 mole) of 40% peracetic acid is added dropwise during 20 minutes, while the flask temperature is maintained at 75 ± 1°C with cooling. The yellow
20 solution is then stirred at 75°C for 45 minutes.

- 25 The flask contents are subjected to reduced pressure to remove the acetic acid, and the residue is refluxed with 400 ml of acetic anhydride for 1 1/2 hours. While the mixture is being heated up, it assumes a dark brown color. The acetic anhydride remaining is then removed under reduced pressure.

- 30 The flask contents are cooled to room temperature, and 500 ml of ethyl ether is added. After adding one liter of water, the organic layer is decanted, and the aqueous layer is extracted thrice with 300 ml portions of ethyl ether. The ether extracts are combined with the organic layer and washed successively with
35 equal volumes of saturated aqueous sodium chloride solution, saturated aqueous sodium bicarbonate, and saturated aqueous sodium chloride solution. The washed material is dried over magnesium sulfate, and the ether is removed by evaporation to obtain 70.0 g
40 of crude product.

- 45 The material is re-extracted with 350 ml of chloroform, the extract is dried over magnesium sulfate, and the chloroform is evaporated to obtain 1.5 g of organic material, of which about one gram is the acetoxy derivative.

- 50 The organic material is distilled in a Vigreux column at 128°—140°C and 2.8—14 mm Hg to obtain 1.0 g of 5-acetoxy-5,6,7,8-tetrahydroquinoxaline.

- 55 The pale yellow liquid boils at 128—129°C at 0.7 mm Hg and has an n_D^{25} of 1.5293. At the 200 ppm level in beef broth it accentuates the brothy aroma. A 2 ppm aqueous solution has a light popcorn flavor note, and a 10 ppm aqueous solution has a popcorn flavor note with a light bitter aftertaste. In peanut butter, this material provides a light roast
60 peanut flavor.

Example II

Preparation of 5-Hydroxy-5,6,7,8-tetrahydroquinoxaline

A 500 ml flask fitted with a mechanical agitator and reflux condenser is charged with 1.5 g of 5-acetoxy-5,6,7,8-tetrahydroquinoxaline and a solution of 12 ml of 20% aqueous potassium hydroxide in 30 ml of methanol. The flask contents are then refluxed for 1 1/2 hours, and thereafter the methanol is stripped away under vacuum. Then 60 ml of water is added, and the resulting liquid is extracted thrice with ethyl ether.

The ether extract is dried over magnesium sulfate, and the ether is stripped off. The 0.7 g residue is dissolved in 4 ml of petroleum ether containing a few drops of ethyl ether and held at 0° to -5°C overnight. The liquid is decanted from the resulting precipitate.

The product is obtained after purification by vacuum distillation as a white solid melting at 64.8—66.0°C. Proton magnetic resonance (PMR) shows an absorption at 8.41 ppm attributable to two aromatic protons; absorption at 4.80 ppm attributable to a proton substituent on a hydroxylated carbon atom adjacent to a pyrazine ring; an absorption at 4.08 ppm attributable to a hydroxyl proton; an absorption at 3.00 ppm attributable to protons in a methylene group adjacent to a pyrazine ring; and adsorption at 2.40—1.70 ppm attributable to the four protons in two methylene groups one carbon atom removed from a pyrazine ring. The odor of a 2 percent alcoholic solution has a fatty, nut-like note and a 6 ppm aqueous solution has a sweet flavor note.

Mass spectroscopy of the material shows a parent peak at 150 and other peaks at 94, 122, 121, and 39.

Example III

Preparation of 5-Oxo-5,6,7,8-tetrahydroquinoxaline

A mixture is prepared by combining 0.50 g (3 millimoles) of 5-hydroxy-5,6,7,8-tetrahydroquinoxaline, 9 ml of dimethyl sulfoxide, and 6 ml of acetic anhydride, and the mixture is then permitted to stand at room temperature (23°C) for 24 hours. At the end of this period the mixture is poured into 50 ml of water and the aqueous layer is extracted thrice with 20 ml portions of methylene chloride. The methylene chloride extracts are combined and acidified with 25 ml of 20% sulfuric acid.

The aqueous layer is separated and washed once with an equal volume of ether. The aqueous layer is then made alkaline with a 20% aqueous potassium hydroxide solution and extracted three times with 15 ml volumes of methylene chloride. The methylene chloride extract is dried over magnesium sulfate, and the solvent is evaporated.

The evaporation leaves 0.40 g of 5-oxo-5,6,7,8-tetrahydroquinoxaline. This material is

a yellow crystalline solid melting at 57.4—59.8°C. PMR shows absorption at 8.64 ppm attributable to two aromatic protons; a triplet at 3.24 ppm attributable to two protons on a methylene group interposed between a methylene group and a carbonyl group adjacent a pyrazine ring; a triplet at 2.84 ppm attributable to two protons in a methylene group adjacent a pyrazine ring; and a quintet at 2.24 ppm attributable to two protons on a methylene group intermediate a methylene group adjacent to a pyrazine ring and a methylene group adjacent to a carbonyl group substituent on a pyrazine ring. Mass spectral analysis of the oxo material shows a parent peak at 148 and other peaks at 119, 92, 120, 41, 39 and 65.

Addition of this material to chicken broth at the 3 ppm level deepens the parsley character. It can be used in spice flavors where light, spicy, earthy flavor notes are desired, e.g., paprika, nutmeg.

Example IV

A cheddar cheese flavoring formulation is prepared by admixing the following ingredients in the amounts indicated:

Ingredient	Amount (parts)
Methyl hexyl keton	1.5
Diacetyl	14.2
isoValeric acid	40.8
Hexanoic acid	158.9
Butyric acid	244.8
Caprylic acid	534.8
Acetyltetrahydroquinoxaline	5.0
produced in Example I	

The foregoing cheese formula is incorporated into a bland cream cheese dip and evaluated. A good strong cheese note is imparted to the dip.

Similarly, other flavors can be improved by adding the acetoxy derivative prepared in Example I or the hydroxy and/or oxo derivatives of Example II and Example III.

II. Preparation And Utilization of Bicyclic Pyrazines:

Example V

Preparation of 5,6,7,8-Tetrahydroquinoxaline
A five-liter Morton flask equipped with an agitator, thermometer, reflux condenser, addition funnel, and gas sparging tube is charged with a solution of 114.2 g (1.0 mole) of 1,2-diaminocyclohexane in 2700 ml of ethanol. The flask contents are cooled to -20°C, and 159.8 g (1.1 mole) of 40% aqueous glyoxal is added during ten minutes. About 2—3 minutes after the addition is complete, the reaction mixture assumes a milky, heterogeneous appearance.

The mixture is then stirred for two hours at -20°C whereafter 40 g of potassium hy-

dioxide pellets are added. Oxygen is passed through the hydroxide-containing mixture for one hour at -20°C, and the temperature is then raised to 40—50°C after which oxygen is passed through for an additional hour. During the higher temperature portion of the oxygen addition the color of the reaction mass changes successively from milky through clear yellow to orange-yellow to darker orange-brown.

The vehicle is recovered in a Buchi evaporator. The brown residue from the evaporator is flash-distilled at 75—88°C and 4.0—2.0 mm Hg to obtain a yellow liquid. The 50.2 g of product in 3000 ml of hexane is then fed to a chromatography column loaded with 1000 g of 80—200 mesh acidified alumina. The column is then successively eluted with 3000 ml of 25% ether-75% hexane, and with 2000 ml of 40% ether-60% hexane to obtain a total of 30.0 g of 5,6,7,8-tetrahydroquinoxaline product.

Proton magnetic resonance (PMR) analysis of the product in carbon tetrachloride shows a broad singlet at 1.92 ppm (four protons on a cyclohexane ring in the beta position from a pyrazine ring), a broad singlet at 2.90 ppm (four protons on a cyclohexane ring alpha to a pyrazine ring), a broad singlet at 2.90 ppm (four protons on a cyclohexane ring alpha to a pyrazine ring), and a singlet at 8.38 ppm attributable to two protons on a pyrazine ring. Infrared (IR) analysis shows absorptions at 3014, 1405, 1154, 1175, 990, 930, 905, 855, and 830 cm⁻¹. Ultraviolet (UV) spectral analysis shows absorptions at 210, 274, and 285 nm.

Mass spectroscopy of the material at an inlet temperature of 150°C, magnet current of 380 ma., ionizing current of 5 µa., and a 70-volt ionizing potential shows:

Mass/Charge	Net Peak Height	Relative Intensity (%)
26	118	18.5
27	157	24.6
39	169	24.5
41	132	20.7
51	114	17.9
52	207	32.5
79	110	17.3
106	179	28.1
119	123	19.3
133	338	53.1
134	637	100.0

Example VI

Preparation of 5,6,7,8-Tetrahydroquinoxaline
A three-necked flask fitted with condenser, mechanical agitator, thermometer, and dropping funnel is charged with 6.0 g of 1,2,3,4-tetrahydrophenazine in 125 ml of water and heated to 90°C, and a solution of 37.0 g of potassium permanganate in 100 ml of water is

added during an hour while the temperature is maintained at 80–90°C. The flask contents are stirred for an additional one-half hour, cooled to 70–75°C, and filtered.

- 5 The residue is slurried in hot water and filtered three times. The filtrates are concentrated to a volume of 200 ml and acidified with 17 ml of concentrated hydrochloric acid. The liquid is then evaporated, and the resulting dicarboxylic acid precipitate is then pyrolyzed in a short-path distillation unit at 200–250°C at 5 mm Hg pressure to substantially pure 5,6,7,8-tetrahydroquinoxaline.

- 15 The aroma of the tetrahydroquinoxaline as perceived from a blotter strip dipped in its alcoholic solutions is oil-fried corn chip fragrance with a potato chip character at the 0.1% level and an earthy popcorn character at the 1.0% level.

- 20 The odor of a 1 ppm solution in water is like fried corn chips, and the taste is like corn chips with a light aftertaste, somewhat reminiscent also of a peanut flavor. At 0.2 ppm in water there is a sweet taste with a light bitter aftertaste. The taste at 0.2 ppm in a 10% aqueous sugar solution is like that of fresh milk with sweet milk chocolate, popcorn, peanut butter, earthy, and coconut flavor notes.

- 30 Tested in beef broth at 4 ppm, the tetrahydroquinoxaline seems to deepen the spice notes and enhances this aspect of the flavor. At 0.5 ppm in chicken broth, the compound adds burning spice notes. Such characteristics fit it for a wide variety of uses as a flavor enhancer and for milk, cream, popcorn, fried corn chips, peanut, hazelnut, chocolate, and coconut flavors and aromas.

Example VII

- 40 Preparation of 2,3-Dimethyl-5,6,7,8-tetrahydroquinoxaline

- A three-liter Morton flask equipped with agitator, thermometer, condenser, addition funnel, gas dispersion tube, and cooling means is charged with 57.0 g (0.5 mol) of 1,2-diaminocyclohexane in 1700 cc of ethanol and cooled to –20°C. During a 20-minute period a solution of 43.0 g (0.5 mol) of 2,3-butanedione in 100 cc of ethanol is added, the flask contents turning milky-white upon such addition. The flask contents are then stirred for 45 minutes at –20°C.

- 55 After this additional stirring is completed, 20.0 g of potassium hydroxide is added, and oxygen is sparged through the mixture for one hour at –20°C. The sparging is continued for 45 minutes as the temperature is permitted to rise to 0°C, whereupon the solution assumes a light brown color, and then for 50 minutes at 40°C. The ethanol is then removed from the clear, dark brown solution under reduced pressure.

The residue after the described ethanol

removal is poured into 750 cc of water and extracted thrice with 250 cc portions of hexane. The hexane extracts are washed twice with equal volumes of saturated aqueous sodium chloride and dried over magnesium sulfate, and the hexane is recovered under reduced pressure. The 56.1 g of material so obtained is distilled in a Vigreux column with no reflux to obtain 26.1 g of a fraction at a pot temperature of 85°C and a vapor temperature of 75°C at a pressure of 0.35 mm Hg.

The aforesaid fraction in the amount of 7.4 g (0.045 mol) is refluxed with 5.0 g of potassium hydroxide in 200 cc of ethanol. The ethanol is then evaporated, and the residue is taken up in ethyl ether. The potassium hydroxide is filtered off, and the crude material is chromatographed on 250 g of aluminum oxide (acid). The column is eluted with 250 cc of hexane and with 500 cc of 40% ether–60% hexane to provide 3.5 g of material.

The 3.5 g is rechromatographed on 100 g of aluminum oxide (acid). Elution with 150 cc of hexane provides no material. Subsequent elution with 500 cc of 40% ether–60% hexane provides 1.76 g of 2,3-dimethyl-5,6,7,8-tetrahydroquinoxaline. This material is a colorless crystalline solid having a tobacco-honey odor and a melting range of 52.2–55.8°C. The structure is confirmed by IR, PMR, and mass spectroscopy.

Other 2,3-dialkyltetrahydroquinoxalines or 2-alkyltetrahydroquinoxalines can conveniently be similarly prepared by utilizing respectively 1,2-dialkyl glyoxals or 1-alkylglyoxals instead of 2,3-butanedione.

Example VIII

Preparation of 5,6,7,8-Tetrahydroquinoxaline

A 250 ml flask equipped with a thermometer, magnetic stirrer, condenser, and addition funnel is charged with 7.2 g of ethylene diamine and 175 ml of diethyl ether and cooled to –50°C. Then 13.2 g of 2-chlorocyclohexanone in 10 ml ether is added during 15 minutes with agitation, and the flask contents are stirred for an additional two hours. Fourteen grams of potassium hydroxide is added and the flask contents are warmed to 3°C.

Air, dried by passage through sulfuric acid, is passed through the reaction mixture for 2.5 hours at 3°C. The reaction mixture is then heated under reflux for an additional one hour and 10 minutes and finally cooled. The course of the oxidation is followed by the gas chromatographic analysis of samples withdrawn from the reaction mixture at various time intervals.

After standing, the reaction mixture is filtered to remove solids and the ether vehicle is stripped off to leave a solid which is distilled under high vacuum using a short path distillation column: The material obtained at 85°C

and 1 mm Hg is further fractionated by gas chromatography to yield pure 5,6,7,8-tetrahydroquinoxaline.

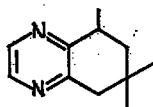
Example IX

5 Preparation of 5,7,7-Trimethyl-5,6,7,8-tetrahydroquinoxaline

A mixture of 6 g (0.1 mol) of ethylenediamine, 15.4 g (0.1 mol) of 2-hydroxy-3,5,5-trimethyl-2-cyclohexen-1-one, 1 g of *p*-toluenesulfonic acid, and one liter of benzene is refluxed for five hours in a three-liter flask fitted with a Bidwell-Sterling distillation receiver. During the refluxing, 3.5 ml of water is collected.

15 After refluxing is completed, the solvent is stripped off, and the residue is dissolved in 300 ml of ethanol. The alcoholic solution is saturated with oxygen for one hour at -20°C , sparged with oxygen for one hour at $40-48^{\circ}\text{C}$, and cooled; and the alcohol is stripped off. The residue after stripping is mixed with 5 g of petroleum oil and vacuum-distilled.

25 The trimethyltetrahydroquinoxaline is obtained as a liquid having a boiling point of 105°C at 1.6 mm Hg and the structure:



30 This material at the 0.6 ppm level in water has a woody, fruity character; at 1 ppm, a nougat, honeylike character; and at 2 ppm a honey, nougat character with a burning taste. The material is particularly interesting for use in honey, tea, nougat, and berry flavors, and is useful in tobacco flavoring compositions.

Example X

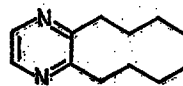
35 Preparation of Pyrazino-[b]-Cyclodecane

Ten grams (0.06 mol) of 1,2-cyclodecadione is refluxed with 4 g of ethylene diamine, one liter of benzene, and 1 g of *p*-toluene sulfonic acid for 2.5 hours. The water formed during the reaction is trapped out, and 2.3 ml is collected. During the refluxing the deep yellow color changes to a light orange color.

40 The reaction mixture is then cooled, and the benzene is stripped off. Ten grams of the product is dissolved in 300 ml of ethanol and 4 g of potassium hydroxide is added. The mixture is cooled to -20°C , and oxygen is passed vigorously through the solution for one hour. The mixture is then warmed to 50°C and oxygen sparging is continued for one hour. The mixture is thereupon cooled, the ethanol is stripped off, and the residue is mixed with "Primol" petroleum oil and distilled under vacuum.

55 The pyrazino[b]cyclodecane is obtained as a yellow liquid having a boiling point of $110-$

112°C at 0.6 mm Hg and the structural formula.



This has a taste at 1 ppm in water of fat-fried onion; at 10 ppm a fat-fried aroma with aftertaste of fresh onion; and at 20 ppm a green vegetable aroma with a fried fat aftertaste. It can be used to provide cereal and heated butter flavor character to consumable products.

Example XI

Cheddar Cheese Flavor Formulation

A cheddar cheese flavoring formulation is prepared by admixing the following ingredients in the amounts indicated:

Ingredient	Amount (parts)	
Methyl hexyl ketone	2	
Diacetyl	10	
isoValeric acid	50	75
Hexanoic acid	200	
Butyric acid	250	
Caprylic acid	600	
Tetra hydroquinoxaline	5	
produced in Example V		80

The foregoing cheese formula is incorporated into a bland cream cheese and, when tested on crackers, is found to have an excellent, sharp cheddar cheese flavor.

Example XII

Beef Soup

The following beef soup-flavoring composition is prepared:

Ingredient	Amount (parts)	
Salt	33.00	90
Hydrolyzed vegetable protein	23.94	
Monosodium glutamate	14.63	
Sucrose	13.33	
Autolyzed yeast powder	4.00	
Onion powder	6.00	95
Beef extract flavor (Example XVI of U.S. Patent 3,394,016)	2.70	
Caramel color powder	2.00	
Celery seed powder	0.27	100
White pepper powder	0.13	

Five ounces of the foregoing mix is added to 8 ounces of boiling water to produce a soup with a beef flavor. This preparation is repeated with a second five-ounce portion in 8 ounces of boiling water to which is added 10 ppm of the tetrahydroquinoxaline prepared in

Example VI. The second preparation containing the tetrahydroquinoxaline is judged to have an improved flavor and aroma with more roast beef flavor character.

5 Example XIII

A beef-flavored gravy is prepared by combining the following materials:

	Ingredient	Amount (parts)
	Water	350
10	Non-fat milk solids	20
	All-purpose flour	16
	Lard	13
	Pregelatinized starch	8
	Margarine	5
15	Bacon fat	5
	Salt	3
	Monosodium glutamate	3
	Sucrose	2
	Hydrolyzed vegetable protein	1
20	Beef extract flavor (per Example VIII of U.S. Patent 3,394,016)	1.6
	Caramel color powder	0.05

25 The foregoing ingredients are homogenized and then autoclaved and a beef gravy is obtained. When 10 ppm of the quinoxaline of Example VI is added, a more pronounced beef flavor character is obtained.

Example XIV

30 A confection center is prepared from the following ingredients:

	Ingredient	(Amount (parts))
	Peanut butter	300
	Ground sweet cracker meal	100
35	Confectioners' sugar	200
	Shortening	25

40 When 5 ppm of the quinoxaline of Example VI is added to the confectionery center composition, a fuller richer flavor character is obtained.

Example XV

45 A commercially available peanut butter is modified to contain 5 ppm of the tetrahydroquinoxaline produced according to the present invention, and the modified peanut butter is tested against the unmodified peanut butter (that is, the peanut butter without added quinoxaline).

50 In panel comparisons of unmodified commercial peanut butter with the modified peanut butter, the modified peanut butter is consistently selected as having a greater peanut butter aroma intensity and a greater peanut taste intensity, with a significance factor of at least 55 95% as calculated by chi-square probability.

Example XVI

Bacon-Flavor Powder

A material useful for providing a bacon flavor to foodstuffs is prepared by admixing the following ingredients:

Ingredient	Amount (parts)	
Salt	45	
Hickory smoke flavor	5	
Furfural	0.1	
Guaiacol	0.1	65
Isoeugenol	0.1	
Ethanol	0.1	
Pelargonic acid	0.1	
Oleic acid	1.0	
Gum arabic	8	70
Water	20	

After the foregoing mixture is prepared 10 ppm of 5,6,7,8-tetrahydroquinoxaline is added, and the mixture is spray-dried in a Bowen-spray-drier. The tetrahydroquinoxaline is described as imparting a nut-like flavor note to the bacon flavor.

III. Preparation And Utilization of Heterocyclic fused. Pyrazines:

Example XVII

Preparation of Methyl Dihydrothienopyrazine
A 500 ml flask is charged with 0.88 g of 3,4-diaminothiophane in 100 ml of 95% ethanol and cooled to -20°C , and a solution of 0.54 g of pyruvic aldehyde in 50 ml of 95% ethanol is added during 15 minutes. After warming to room temperature 0.27 g of sodium hydroxide in 20 ml of 95% ethanol is added, and the mixture so formed is heated at reflux for two hours. After cooling, solvent removal *in vacuo* gives a brown tar. Trituration with methylene chloride, followed by solvent removal *in vacuo*, gives 0.70 g of residue. Column chromatography followed by preparative gas chromatography gives a white crystalline sample of 2-methyl-5,7-dihydrothieno-[3,4-b]pyrazine.

Mass spectroscopy of the white crystalline solid so produced shows peaks at *m/e* ratios of 152, 151, 39, 41, and 57. UV (ultraviolet) spectroscopy shows λ_{max} at 213 and 276 *mμ* with a shoulder at 307 *mμ*. PMR (proton magnetic resonance) in deuteriochloroform shows a singlet at 8.24 accounting for one proton, a singlet at 4.23 accounting for four protons, and a singlet at 2.55 accounting for three protons. This substance has a roasted nut aroma. It can be used in flavoring food and tobacco products, both to provide popcorn or roast cereal flavor notes and to enhance and 110 interact with other fragrances and flavor notes.

Example XVIII

Preparation of Dihydrodimethylfuropyrazine

A three-neck reaction flask fitted with a gas-inlet, thermometer, magnetic stirrer, and drying tube is charged with 2.0 g (0.0073 moles) of 2,5-dibromo-3,4-hexanedione in 20 ml of methanol. The mixture is cooled to -10°C with stirring, and 0.44 g (0.0073 moles) of 1,2-diaminoethane is added. The temperature rises to -5°C during the addition, and the reaction mixture is then stirred at -10°C to -20°C for two hours.

A pellet of potassium hydroxide is added and air is bubbled through the mixture. The mixture is permitted to reach room temperature while the air is being added, and an additional small quantity of a solution of sodium hydroxide in methanol is added. The air bubbling is continued for an additional eight hours.

The oxygenated mixture so obtained is poured into 10 ml of water and pH is adjusted to 8 with 20% aqueous hydrochloric acid. This mixture is then extracted five times with 50 ml portions of methylene chloride. The extracts are dried over sodium sulfate, filtered, and concentrated to obtain 0.5 g of a dark brown oil.

The oil is resolved by gas-liquid chromatography (GLC) to obtain 5,7-dihydro-5,7-dimethylfuro[3,4-b]pyrazine. This material has a sweet roasted aroma in a one percent ethanol solution. PMR analysis confirms its structure.

In a one ppm aqueous solution, this material is near the threshold level of its taste; in 3 ppm aqueous solution it has a popcorn flavor note; and at 10 ppm it shows a roasted nut character, reminiscent of hazlenut and peanut. At 10 ppm in a 10 percent aqueous sucrose solution, it provides a dominating roasted nut character. At 3 ppm in 4 percent aqueous salt solution it has a yeasty roasted taste, while at 10 ppm it has a salted roast nut taste.

A chicken broth is prepared, and 3 ppm of the material of Example XVIII is added. The aroma and taste of roast chicken are imparted to the broth, and the general taste of the broth is improved. A beef broth is prepared, and 10 ppm of the material of Example XVIII is added. The material imparts a baked potato character to the broth. This furo-pyrazine is judged to be suitable for imparting roasted flavor notes to peanuts, and is also suitable for malt flavors.

Example XIX

Preparation of Dihydrothienopyrazine

To a refluxing solution of 5.6 g of sodium hydrosulfide in 300 ml of methanol is added a solution of 8.8 g 2,3-di(chloromethyl)pyrazine in 25 ml methanol during ten minutes. After refluxing for an additional 1.5 hours, the reaction mixture is allowed to stand at room

temperature (about 23°C) for 70 hours, and then refluxing is repeated for an additional three hours.

The mixture is cooled to room temperature and the methanol is removed to provide a dark brown solid. This solid is extracted with 300 ml methylene chloride, and the methylene chloride is removed in vacuo to provide 5.3 g of a brown oil.

The oil is chromatographed several times on silicic acid with methanol/methylene chloride mixture to provide a product which upon crystallization from a 95% ethanol solution yields 0.18 g of 5,7-dihydrothieno[3,4-b]pyrazine.

This thienopyrazine derivative is a solid melting at $86-89^{\circ}\text{C}$. Sublimation in vacuo provides 0.10 g of material melting at $88-89^{\circ}\text{C}$. Mass spectroscopy shows peaks at m/e ratios of 138, 137, 57, 41, 29, and 39. UV analysis shows a λ_{max} at 211 and 255 $m\mu$ with a shoulder at about 309 $m\mu$. PMR in deuteriochloroform shows a singlet at 8.36 accounting for two protons and a singlet at 4.26 accounting for four protons.

The odor of a 0.01 percent solution of this material in 95% ethanol is near the threshold level and is light roasted nut with a popcorn-like note; at 0.1 percent in such ethanol, the odor is roasted nut, especially redolent of peanut and hazlenut. The taste of this material in water at the 0.02 ppm level is characteristic of roasted peanut, bread crust, with an odor reminiscent of fresh milk; at 0.2 ppm, a baked goods, bread crust, roasted nut taste; at 2 ppm, a sweet characteristic nut flavor with no bitter aftertaste.

In sucrose solution at 4 ppm the dihydrothienopyrazine has a flavor like baked goods, while at 3 ppm in salt water there is a fried corn chip, salted peanut flavor character. This pyrazine derivative is suitable for roasted nut flavors, baked goods flavors, and other flavors.

Example XX

A cheddar cheese flavoring formulation is prepared by admixing the following ingredients in the amounts indicated:

Ingredient	Amount (parts)	
Methyl hexyl ketone	1.5	
Diacetyl	14.2	
isoValeric acid	40.8	
Hexanoic acid	158.9	
Butyric acid	244.8	115
Caprylic acid	534.8	
Dihydrothienopyrazine produced in Example XVII	5.0	

The foregoing cheese formula is incorporated into a bland cream cheese spread and evaluated on crackers. A good sharp cheddar flavor is imparted to the cheese spread.

IV. Preparation And Utilization of Bicyclic Dehydropiperazines.

Example XXI

Preparation of 4a,5,6,7,8,8a-Hexahydroquinoxaline

5 A five-liter Morton flask equipped with an agitator, thermometer, reflux condenser, addition funnel, and gas sparging tube is charged with a solution of 114.2 g (1.0 mole) of 1,2-diaminocyclohexane in 2700 ml of 95% ethanol. The flask contents are cooled to -20°C, and 159.8 g (1.1 mole) of 40% aqueous glyoxal is added during ten minutes. About 2—3 minutes after the addition is complete, the reaction mixture assumes a milky, heterogenous appearance. The mixture is then stirred for two hours at -20°C.

15 The resulting mixture is found to have an intense popcorn aroma. The mixture is found by mass spectroscopy to contain the 20 4a,5,6,7,8,8a-hexahydroquinoxaline.

Example XXII

Preparation of 5-Methyl-3,4,6,7-tetrahydro-2(H)-cyclopentapyrazine

25 A reaction mixture is prepared by dissolving 12.4 g 3-methyl-2-hydroxy-2-cyclopenten-1-one (the enol form of 3-methyl-1,2-cyclopentadione) in 10 g of ethylene diamine. The mixture is then stirred at room temperature (23°C) and an exothermic reaction takes place. The mixture thickens and after two hours forms a solid crystalline mass.

30 The solid mass is dissolved in 50 ml of methylene chloride and washed with 10 ml of water. The water layer is back-washed with an equal volume of methylene chloride, and the combined methylene chloride solutions are evaporated to dryness to yield 15.2 g of a crystalline mass having a bread, nut-like aroma. The product is purified by sublimation.

35 The product obtained is 5-methyl-3,4,6,7-tetrahydro-2(H)-cyclopentapyrazine. Infrared (IR) analysis indicates an NH band, and mass spectroscopy shows a molecular weight of 136. 45 The material has a good nut-like aroma suggestive of tobacco and burns well with natural tobacco. The odor is also similar to that of fresh baked goods in a one percent solution in 95% ethanol. The taste in water at 5 ppm is near the threshold level with a pleasant, sweet, light roasted, buttery note. A 20 ppm aqueous solution has a melted butter flavor character; a 50 ppm solution, a bread-crust character. A 50 ppm solution in sugar water 55 has a flavor like fresh sugar cookies or fresh corn flakes. In salt water at 50 ppm it has a taste reminiscent of fresh baked pretzels, with a bread-crust flavor note.

Example XXIII

Preparation of 2,3-Dimethyl-4a,5,6,7,8,8a-hexahydroquinoxaline

A Morton flask equipped with agitator,

thermometer, condenser, addition funnel, gas dispersion tube, and cooling means is charged with 11.40 g of 1,2-diaminocyclohexane in 200 cc of 95% ethanol. During a 20-minute period a solution of 816 g of 2,3-butanedione is added dropwise. The temperature rises from 25° to 37°C and the flask contents turn milky-white upon such addition. The reaction mixture turns clear after 15 minutes.

The ethanol is removed by evaporation under reduced pressure and the residue is distilled under vacuum yielding 16.1 g of product boiling at 72—76°C at 1.4—1.7 mm Hg. Gas chromatographic (GC) analysis shows a mixture of the *cis* and *trans* isomers, and the material has a broad melting range of 60° to 110°C. Initially a white solid, the product discolors on storage.

The material has a cedar wood, tobacco, buttery odor. In chocolate beverages it imparts a bitter character without the addition of any foreign flavor note. In a soap bouquet perfume composition, the compound can be used to replace natural cedarwood.

Other 2,3-dialkylhexahydroquinoxalines or 2-alkylhexahydroquinoxalines can be similarly prepared by utilizing other 1,2-dialkyl glyoxals or 1-alkylglyoxals instead of 2,3-butanedione.

Example XXIV

Preparation of 5,7,7-Trimethyl-2,3,4,6,7,8-hexahydroquinoxaline

A mixture of 6 g (0.1 mol) of ethylenediamine and 15.4 g (0.1 mol) of 2-hydroxy-3,5,5-trimethyl-2-cyclohexen-1-one (the enol form of 3,5,5-trimethyl-1,2-cyclohexandione) is refluxed for five hours in one liter of benzene in a three-liter flask fitted with a Bidwell-Sterling distillation receiver. During the refluxing, 3.5 ml of water is collected. After refluxing is completed, the solvent is stripped off.

The resulting trimethyl substituted reduced bicyclic pyrazine has a tobacco, nougat aroma in a 0.2 percent solution in 95% ethanol. In aqueous solution at 0.4 ppm it has a fruity taste with tobacco leaf and cedarwood notes. It is suitable for honey, nougat, and tobacco flavors.

Example XXV

Preparation of 2,3,5,6,7,8,9,10,11,12-Decahydrocyclodecapyrazine

A mixture of 3.8 g of 1,2-cyclodecadione, 2.0 g of ethylene diamine, and 200 ml of benzene is refluxed in a 250 ml round bottom flask equipped with a Bidwell trap and condenser. During a 2.5-hour period one milliliter of water is collected.

After the reaction, the flask contents are cooled and the benzene is stripped off. PMR and mass spectral analyses confirm the production of the decahydrocyclodecapyrazine. The material so produced has nut-like and fatty flavor.

Example XXVI**Preparation of 5-Methyl-2,3,6,7-tetra-cyclopentapyrazine**

5 A five-liter flask equipped with a stirrer, a Bidwell trap, and a condenser is charged with three liters of benzene, 116 g of 3-methyl-2-hydroxy-2-cyclopenten-1-one, and 72 g of 91-93% ethylene diamine. In 2.5 hours, 46 ml of water is collected.

10 The flask contents are cooled, the benzene is stripped off in a Büchi apparatus, and the solid residue is held under vacuum overnight to remove all traces of benzene.

15 A thirty gram portion of the product is sublimed to provide about 12 g of purified product.

Example XXVII

20 A cheddar cheese flavoring formulation is prepared by admixing the following ingredients in the amounts indicated:

	Ingredient	Amount (parts)
	Methyl hexyl ketone	2
	Diacetyl	10
	isoValeric acid	50
25	Hexanoic acid	200
	Butyric acid	250
	Caprylic acid	600
	Compound prepared in Example XXII	5

30 The foregoing cheese formula is incorporated into a bland cream cheese and, when tested on crackers, is found to have an excellent, sharp cheddar cheese flavor.

Example XXVIII
Beef Soup

35 The following beef soup-flavoring composition is prepared:

	Ingredient	Amount (parts)
40	Salt	33.00
	Hydrolyzed vegetable protein	23.94
	Monosodium glutamate	14.63
	Sucrose	13.33
	Autolyzed yeast powder	4.00
45	Onion powder	6.00
	Beef extract flavor (Example XVI of U.S. Patent 3,394,016)	3.30
	Caramel color powder	2.00
	Celery seed powder	0.27
50	White pepper powder	0.13

55 Five ounces of the foregoing mix is added to 8 ounces of boiling water to produce a soup with a beef flavor. This preparation is repeated with a second five-ounce portion in 8 ounces of boiling water to which is added 10 ppm of the product of Example XXII. The second preparation containing the pyrazine is judged

to have improved flavor and aroma with more beef flavor character.

Example XXIX

60 A beef-flavored gravy is prepared by combining the following materials:

Ingredient	Amount (parts)	
Water	350	
Non-fat milk solids	20	65
All-purpose flour	16	
Lard	13	
Pregelatinized starch	8	
Margarine	5	
Bacon fat	5	70
Salt	3	
Monosodium glutamate	3	
Sucrose	2	
Hydrolyzed vegetable protein	1	
Beef extract flavor (per Example VIII of U.S. Patent 3,394,016)	1.6	75
Caramel color powder	0.05	

The foregoing ingredients are homogenized and then autoclaved. A beef gravy is obtained. When 10 ppm of the pyrazine of Example XXII is added, a more pronounced beef flavor character is obtained.

Example XXX

85 A confection center is prepared from the following ingredients:

Ingredient	Amount (parts)	
Peanut butter	300	
Ground sweet cracker meal	100	
Confectioners' sugar	200	
Shortening	25	90

When 5 ppm of the product of Example XXII is added to the confectionery center composition, a fuller, richer flavor character is obtained.

Example XXXI**Bacon-Flavor Powder**

A material useful for providing a bacon flavor to foodstuffs is prepared by admixing the following ingredients: 100

Ingredient	Amount (parts)	
Salt	45	
Hickory smoke flavor	5	
Furfural	0.1	
Guaiacol	0.1	105
Isoeugenol	0.1	
Ethanol	0.1	
Pelargonic acid	0.1	
Oleic acid	1.0	
Gum arabic	8	110
Water	20	

After the foregoing mixture is prepared 10 ppm of the pyrazine of Example XXIV is added, and the mixture is spray-dried in a Bowen spray-drier. This bicyclic dehydropiperazine imparts a nut-like flavor note to the bacon flavor.

Example XXXII Perfume Composition

A "bouquet" type of perfume composition is prepared by admixing the following ingredients:

Ingredient	Amount (parts)
Terpineol	200
Rosewood	200
15 Lavender Spike	100
Diphenyl oxide	30
Material produced in Example XXIV	100
Citronella, Java	200
20 Clove	50
Linalyl acetate	50
Red thyme	20
Styrax	20
Musk xylene	30

The material of Example XXIV is used in the foregoing perfume composition in lieu of an equal amount of natural cedarwood, and the composition is found to have substantially the same odor quality as would be obtained with natural cedarwood.

V. Preparation And Utilization of Tricyclic Pyrazines:

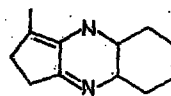
Example XXXIII

Preparation of 1-Methyl-2,3,5,6,7,8-hexahydro-1(H)-cyclopenta[b]quinoxaline

A three-liter flask equipped with condenser, stirrer, heater, and Bidwell trap, is charged with the following ingredients:

Ingredient	Amount
40 Cyclotene (3-methyl-1,2-cyclopentanediol)	34.8 g
1,2-Diaminocyclohexane	34.2 g
P-Toluene sulfonic acid	2 g
Anhydrous benzene	1.5 liters

The mixture is refluxed at atmospheric pressure for three hours, during which time 12 ml of water is collected in the Bidwell trap. The reaction mass is then cooled and the benzene is stripped off at reduced pressure. The 53 grams of solid residue materials is then sublimed to obtain 29 grams of 1-methyl-3,4a,5,6,7,8,8a,9-octahydro-2(H)-cyclopenta[b]quinoxaline having the structure:

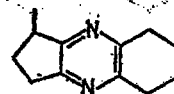


The structure is confirmed by proton magnetic resonance (PMR) analysis.

Ten grams of the material produced above is charged to a one-liter flask, together with 38 ml of ethanol and 2 g of solid potassium hydroxide. The reaction mixture is cooled to 20°C, and oxygen is bubbled into the mixture for one hour. The oxygen-saturated reaction mass is then heated to 50°C, and oxygen is again bubbled in for another hour, while the reaction mass is maintained at 50°C. The reaction mass is cooled, the ethanol is stripped off at reduced pressure, and the residue is then extracted with four 150 ml volumes of ether and washed with 100 ml of saturated sodium chloride solution.

The ether extract is dried over anhydrous magnesium sulfate and the dried solution is stripped of ether.

The resulting solid material has a nut-like aroma and the following structure:



As confirmed by PMR and mass spectral analysis.

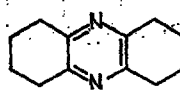
Example XXXIV

Preparation of 1,2,3,4,6,7,8,9-Octahydrophenazine

A two-liter flask equipped with condenser, stirrer, and Bidwell trap is charged with the following ingredients:

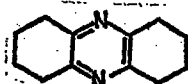
Ingredient	Amount
Cyclohexane-1,2-dione	9.65 g
1,2-Diaminocyclohexane	11.4 g
P-Toluene sulfonic acid	1.0 g
Benzene, anhydrous	1 liter

The reaction mass is heated at reflux for two hours until 3.6 ml of water is collected in the Bidwell trap. The reaction mass is thereupon cooled, and the benzene is stripped from the reaction mass at reduced pressure to obtain 15 grams of 1,2,3,4,4a,6,7,8,9,10a-decahydrophenazine having the structure:



This structure is confirmed by PMR and infrared (IR) analyses.

A one-liter flask is charged with 15 g of the decahydrophenazine dissolved in 300 ml of 95% ethanol, 4 g of potassium hydroxide is added, and oxygen is bubbled into the reaction mass for one hour at -20°C and then for one hour at 50°C . The reaction mass is cooled, dissolved in water, and extracted with diethyl ether. The ether extract is evaporated and the residue is dissolved in 160 ml of 95% ethanol. Six grams of potassium hydroxide are added to the alcoholic solution and the mixture is refluxed for four hours whereafter the mixture is cooled and the ethanol is stripped off to provide a white solid. This solid is extracted with three 150 ml volumes of diethyl ether, and the ether extract is washed with the saturated sodium chloride solution. The ether extract is dried over anhydrous magnesium sulfate and stripped of ether. The resulting 4 g is distilled at a temperature in the range of $125^{\circ}\text{--}130^{\circ}\text{C}$ and a pressure of 2.0–2.5 mm Hg. NMR, IR and mass spectral analysis confirm the structure:



The yellowish viscous liquid has the taste of fried corn chips at a level of 5 ppm.

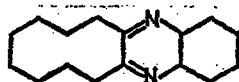
Example XXXV

Preparation of 1,2,3,4,6,7,8,9,10,11,12,13-Dodecahydrocycloclodeca-[b]quinoxaline

A 2-liter reaction vessel equipped with stirrer, reflux condenser, and Bidwell trap is charged with:

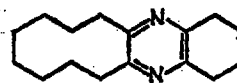
Ingredient	Amount
Cyclodecane-1,2-dione	10 g
1,2-Diaminocyclohexane	6.6 g
P-Toluene sulfonic acid	1.5 g
Benzene, anhydrous	1 liter

The mixture is refluxed for two hours until 2.5 ml of water is collected in the Bidwell trap. The reaction mass is then cooled and the benzene stripped off to yield 21 g of a solid residue. This material is determined by mass spectral analysis and PMR to be the reduced pyrazine having the structure:



The 21 grams of solid is dissolved in 250 ml of ethanol in a 1-liter flask, 6 grams of potassium hydroxide is added, and the reaction mixture is refluxed for three hours and then cooled. The ethanol is stripped off and the residue

dissolved in 100 ml of saturated sodium chloride solution. The sodium chloride solution is extracted four times with 150 ml portions of ether. The extracts are combined and then dried over anhydrous magnesium sulfate. The dried ether extract is stripped of ether. The resulting 21 g of residue is distilled at a temperature in a range of $160\text{--}166^{\circ}\text{C}$ at 2 mm Hg. PMR, IR and mass spectral analysis shows that the material is 1,2,3,4,6,7,8,9,10,11,12,13-dodecahydrocycloclodeca[b]quinoxaline having the structure:



This material has a light, sweet, nut character.

Example XXXVI

A basic cocoa flavor material is prepared by admixing the following materials:

Ingredient	Amount	
Acetaldehyde	20.0	
Isobutyraldehyde	16.0	70
Isovaleraldehyde	40.0	
Methyl sulfide	0.35	
Methyl disulfide	0.44	
Isobutyl acetate	0.12	
Isoamyl acetate	0.20	75
Phenylethyl acetate	0.59	
Diacetyl	0.02	
Acetophenone	1.00	
Furfural (50%)	0.06	
Benzaldehyde	1.00	80
Phenylacetaldehyde	0.58	
Isoamyl alcohol	0.18	
Phenylethyl alcohol	3.50	
γ -Butyrolactone	0.13	
	84.17	85

A nut-like flavor note material is prepared by combining the following ingredients as shown:

Ingredient	Amount (parts)	
Material produced in Example XXXIII	11.0	90
Material produced in Example XXXIV	27.0	
Material produced in Example XXXV	20.0	95
	58.0	

A first flavor composition is prepared by a 1.2% dilution of the basic cocoa flavor in propylene glycol/ethyl alcohol (v/v 80/20). Vanillin is added in the ratio of 250 mg. per kilogram of solution. A second flavor composition

tion is prepared by a 2% dilution of the basic cocoa flavor combined with the nut-like flavor note material (weight ratio 84.2:58.0) in propylene glycol/ethyl alcohol (v/v 80/20).
5 Vanillin is added in the ratio of 250 mg. per kilogram of liquid.

The combined flavor (2% dilution) thus prepared is found to have an excellent cocoa flavor and aroma note, whereas the flavor without the tricyclic pyrazines of this invention lacks the desirable nut-like flavor note.
10

Example XXXVII

The pyrazine-containing flavor note material of Example XXXVI is added to a commercially available chocolate flavored dessert containing skim milk, sugar, non-fat dry milk solids, and cocoa with a bland, thin cocoa flavor. The addition of 63 mg/kg increases the nut-like note to a desirable level and improves the overall flavor.
15
20

It will be appreciated from this disclosure that other alkyl-substituted and unsubstituted tricyclic pyrazines can be used in lieu of or addition to the materials shown above with favorable results.
25

Example XXXVIII

A flavor composition according to this invention is prepared by combining the following materials as shown:

30	Compound	Amount (grams)
	Tricyclic pyrazine of Example XXXIII	6
	Tricyclic pyrazine of Example XXXIV	15
35	Tricyclic pyrazine of Example XXXV	12

This tricyclic pyrazine composition is added to a chocolate milk having a bland, thin cocoa flavor. Adding 30 mg/kg increases the nut-like note, and supplemental addition of 40 mg/kg of the basic cocoa flavor material as described in Example XXXVI gives the chocolate milk an excellent cocoa flavor and aroma note.
40

Example XXXIX

A commercial cocoa mix is used to prepare two different batches of beverage. The first batch is evaluated without any further additive, while the material of Example XXXIII is added to the second batch in the ratio of 40 mg of the tricyclic pyrazine to each kilogram of cocoa beverage. The beverage without tricyclic pyrazine gives a rather harsh flavor impression, while the beverage containing tricyclic pyrazine according to the present invention has a fuller, richer cocoa flavor.
45
50
55

Example XL

The aroma provided by the 1,2,3,4,6,7,8,9-

octahydrophenazine (as produced in Example XXXIV) in the composition set forth below is important to the "natural" undertone quality of certain floral absolutes such as Hyacinth and Narcissus. The formulation is as follows:
60

Ingredient	Amount	
Phenylacetylaldehyde	150	65
Tolubalsamol	50	
Phenylethylalcohol	150	
Cinnamyl alcohol from Styxax	200	
Hydroxycitronellal	80	70
Heliotropin	50	
Terpineol	30	
Petitgrain bigarade	40	
Benzylacetate over Jasmin	150	75
Benzylacetate, extra	100	
Benzylbutyrate	10	
Linalool, extra	100	
Hyacinth absolute	10	80
Benzylacetate	10	
Cinnamylacetate	30	
Phenylethylacetate	20	
α -Ionone	20	85
Isoeugenol, extra	5	
Jasmin absolute	10	
Rose de Mai absolute	10	
Neroli, extra	10	85
γ -n-Methylionone	15	
Phenylethylalcohol	120	
Jasmin Chassis absolute	5	
Eugenol	3	90
1,2,3,4,6,7,8,9-Octahydrophenazine	1	

The addition of the 1,2,3,4,6,7,8,9-octahydrophenazine lends an authentic, earthy, dank character bringing the composition closer to the odor of pure Hyacinth absolute.
95

Example XLI

A perfume composition is prepared by admixing the following ingredients:

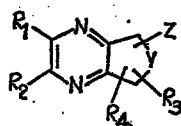
Ingredient	Amount	100
Guaiac wood oil	40	105
8,9-Epoxycedrane	20	
Octahydro-3,6,8,8-tetramethyl-1H-3a,7-methanoazulen-6-ol (Cedrenol)	20	
Methyl-3,6,7,8-tetramethyl-1H,3a,7-methanoazulen-6-yl-ketone (Cedryl methyl ketone)	6	
Ortho-t-butylcyclohexanol	3	110
1,2,3,4,6,7,8,9-Octahydrophenazine (10% solution in 95% ethanol)	1	

The small amount of 1,2,3,4,6,7,8,9-octahydrophenazine significantly improves the total effect of the fragrance imparting the necessary rooty, potato-like nutty character to the mixture of the other woody materials.
115

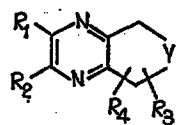


WHAT WE CLAIM IS:—

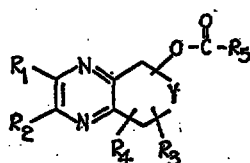
1. A pyrazine material represented by any of the Formulae designated I, II, III, IVA or IVB herein.
2. A process for altering the flavor of a consumable material which comprises adding thereto a small but effective amount of at least one pyrazine material represented by any of the Formulae I, II, III, IVA or IVB herein.
3. Oxycyclic pyrazines having the formula



- wherein Y is $-\text{CH}_2-$ or $-\text{CH}_2-\text{CH}_2-$; Z is a carbonyl oxygen, a hydroxyl group, or an acyloxy group having from two to four carbon atoms; and R_1 , R_2 , R_3 , and R_4 are the same or different and represent hydrogen or lower alkyl having one to three carbon atoms.
4. An oxycyclic pyrazine according to Claim 3 wherein Y is $-\text{CH}_2-\text{CH}_2-$; Z is a carbonyl oxygen; and R_1 , R_2 , R_3 , and R_4 are hydrogen.
 5. An oxycyclic pyrazine according to Claim 3 wherein Y is $-\text{CH}_2-\text{CH}_2-$; Z is hydroxy; and R_1 , R_2 , R_3 , and R_4 are hydrogen.
 6. An oxycyclic pyrazine according to claim 3 wherein Y is $-\text{CH}_2-\text{CH}_2-$; Z is acetyloxy; and R_1 , R_2 , R_3 , and R_4 are hydrogen.
 7. A process for altering the flavor of a consumable material which comprises adding thereto a small but effective amount of at least one oxycyclic pyrazine according to claim 3.
 8. A process for the production of oxycyclic pyrazines which comprises oxidizing a cyclic pyrazine having the formula



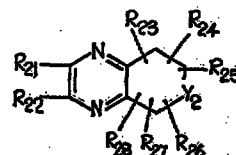
- wherein Y is $-\text{CH}_2-$ or $-\text{CH}_2-\text{CH}_2-$ and R_1 , R_2 , R_3 , and R_4 are hydrogen or lower alkyl having one to three carbon atoms with a peracid to obtain an oxidized product and treating the oxidized product with a lower (C_2-C_4) alkanolic acid anhydride to obtain a material having the structure



- wherein Y, R_1 , R_2 , R_3 , and R_4 are as set forth

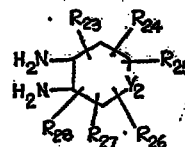
above and R_5 is lower alkyl having one to three carbon atoms.

9. Bicyclic pyrazines having the formula



wherein Y_2 is $(-\text{CH}_2-)_n$; n is an integer from 1 to 5, inclusive; and R_{21} , R_{22} , R_{23} , R_{24} , R_{25} , R_{26} , R_{27} , and R_{28} are the same or different and represent hydrogen or lower alkyl having one to three carbon atoms.

10. A bicyclic pyrazine according to Claim 9 wherein n is 1 and R_{21} , R_{22} , R_{23} , R_{24} , R_{25} , R_{26} , R_{27} , and R_{28} are hydrogen.
11. A bicyclic pyrazine according to Claim 9 wherein n is 1, R_{21} and R_{22} are methyl, and R_{23} , R_{24} , R_{25} , R_{26} , R_{27} , and R_{28} are hydrogen.
12. A bicyclic pyrazine according to Claim 9 wherein n is 1, R_{24} and R_{25} are methyl groups substituent on the ring carbon atom immediately above Y_2 , R_{26} is a methyl group substituent on the other carbon atom adjacent to Y_2 , and R_{21} , R_{22} , R_{23} , R_{27} , and R_{28} are hydrogen.
13. A bicyclic pyrazine according to Claim 9 wherein n is 5 and R_{21} , R_{22} , R_{23} , R_{24} , R_{25} , R_{26} , R_{27} , and R_{28} are hydrogen.
14. A process for altering the flavor of a consumable material which comprises adding thereto a small but effective amount of at least one bicyclic pyrazine according to Claim 9.
15. A process for preparing a bicyclic pyrazine according to Claim 9 which comprises reacting a 1,2-diaminocycloalkane having the formula



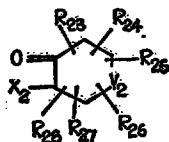
with a dioxoalkane having the formula



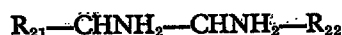
at a temperature below the freezing point of water to produce a hydropyrazine bicyclic compound and dehydrogenating the latter to provide the bicyclic pyrazine.

16. A process according to Claim 15 wherein the temperature of the reaction with diamino-cycloalkane is from -80°C to -10°C .
17. A process for preparing a bicyclic pyrazine according to Claim 9 which com-

prises reacting a 2-halocycloalkanone having the formula

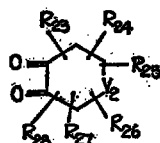


- 5 (wherein X_2 is a halogen) with a diaminoalkane having the formula



- 10 at a temperature from -80° to $+10^\circ\text{C}$ to produce a hydropyrazine bicyclic compound (or mixture of isomers thereof), and dehydrogenating the latter to provide a bicyclic pyrazine.

- 15 18. A process for preparing a bicyclic pyrazine according to Claim 9 which comprises reacting a 1,2-cycloalkadione having the formula



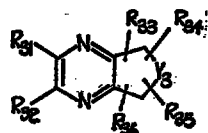
with a diaminoalkane having the formula



- 20 at a temperature of from 50° to 100°C to produce a hydropyrazine bicyclic compound (or mixture of isomers thereof), and dehydrogenating the latter to provide a bicyclic pyrazine.

- 25 19. A process for the production of a 5,6,7,8-tetrahydroquinoxaline which comprises oxidizing a 1,2,3,4-tetrahydrophenazine to form tetrahydroquinoxaline 1,2-dicarboxylic acid and pyrolysis of the acid to produce the tetrahydroquinoxaline.

- 30 20. Heterocyclic fused pyrazines having the formula



- 35 wherein Y_3 is $-O-$, $-S-$, $-CH_2-S-$, or $-CH_2-O-$ and R_{31} , R_{32} , R_{33} , R_{34} , R_{35} , R_{36} are the same or different and represent hydrogen or lower alkyl having one to three carbon atoms.

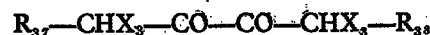
21. 2 - methyl - 5,7 - dihydrothieno - [3,4-b]-pyrazine.

22. 5,7 - dihydro - 5,7 - dimethylfuro - [3,4-b]-pyrazine.

23. A process for altering the flavor of a consumable material which comprises adding thereto a small but effective amount of at least one heterocyclic pyrazine according to claim 20.

24. A process for preparing dihydrothienopyrazines which comprises reacting a 3,4-diaminothiophane or a mono- or dialkyl substituted 3,4-diaminothiophane with an α -diketone in the presence of an alkali metal hydroxide and subsequently dehydrogenating the reaction product.

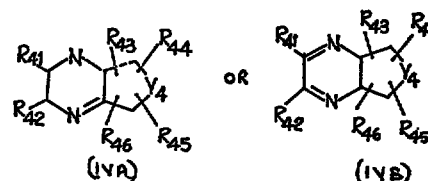
25. A process for preparing dihydrofuro-pyrazines which comprises reacting a dione having the formula



- wherein each X_3 is a halogen atom and R_3 and R_4 are hydrogen or lower alkyl having one to three carbon atoms, with 1,2-diaminoethane, 1-alkyl-1,2-diaminoethane, or 1,2-dialkyl-1,2-diaminoethane, and oxidizing the resulting intermediate product to obtain the furopyrazine.

26. A process for preparing dihydrothienopyrazines which comprises reacting an alkali metal hydrosulfide with a 2,3-di(haloalkyl)-pyrazine at a temperature of from $50-100^\circ\text{C}$.

27. Bicyclic dehydropiperazines having the formula:



wherein Y_4 is $(-CH_2-)_{n_4}$; n_4 is an integer from one to six; one of the dashed lines is a double bond and the other dashed line is a single bond; and R_{41} , R_{42} , R_{43} , R_{44} , R_{45} and R_{46} are the same or different and represent hydrogen or lower alkyl having one to three carbon atoms.

28. A bicyclic dehydropiperazine according to formula IVA of Claim 27 wherein n_4 is one; R_{41} , R_{42} , R_{43} , R_{44} , R_{45} , and R_{46} are hydrogen; and R_{46} is methyl substituent on the carbon atom between Y_4 and the dashed line.

29. A bicyclic dehydropiperazine according to Claim 27 wherein n_4 is two; R_{41} and R_{42} are methyl and R_{43} , R_{44} , R_{45} and R_{46} are hydrogen.

30. A bicyclic dehydropiperazine according to Claim 27 wherein n_4 is two; R_{45} and R_{46} are methyl groups substituent on the ring car-

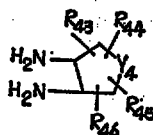


bon atom immediately below Y_4 ; R_{43} is a methyl group substituent on the other carbon atom adjacent to Y_4 ; and R_{41} , R_{42} , R_{44} are hydrogen.

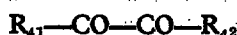
- 5 31. A bicyclic dehydropiperazine according to Claim 27 wherein n_4 is six and R_{41} , R_{42} , R_{43} , R_{44} , R_{45} , and R_{46} are hydrogen.

- 10 32. A process for altering the flavor of a consumable material which comprises adding thereto a small but effective amount of at least one bicyclic dehydropiperazine according to Claim 27.

- 15 33. A process for preparing a bicyclic dehydropiperazine according to Claim 27 which comprises reacting a diaminocycloalkane having the formula

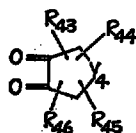


with a dioxoalkane having the formula



- 20 at a temperature of from $-80^{\circ}C$ to $50^{\circ}C$ to produce a bicyclic dehydropiperazine compound.

- 25 34. A process for preparing a bicyclic dehydropiperazine according to Claim 27 which comprises reacting a 1,2-cycloalkadione having the formula

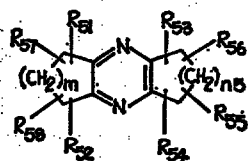


with a diaminoalkane having the formula



- 30 wherein R_{41} and R_{42} are hydrogen or lower alkyl having one to three carbon atoms and are the same or different; at a temperature of from 50° to $150^{\circ}C$ to produce a bicyclic dehydropiperazine compound.

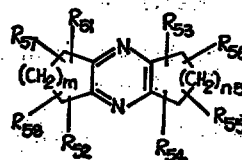
- 35 35. A process for altering the flavor of a consumable material which comprises adding thereto a small but effective amount of at least one tricyclic pyrazine having the formula:



- 40 wherein m and n_5 are the same or different and

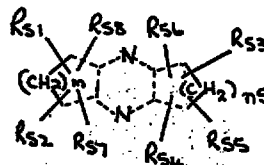
are integers from one to six, inclusive, and R_{51} , R_{52} , R_{53} , R_{54} , R_{55} , R_{56} , R_{57} , and R_{58} are hydrogen or lower alkyl having one to three carbon atoms.

36. A process for altering the fragrance of a composition by adding to the composition a small but effective amount of at least one tricyclic pyrazine having the formula:



wherein m and n_5 are the same or different and are integers from one to six, inclusive, and R_{51} , R_{52} , R_{53} , R_{54} , R_{55} , R_{56} , R_{57} , and R_{58} are hydrogen or lower alkyl having one to three carbon atoms.

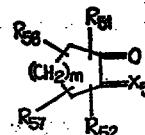
37. A chemical compound having the formula:



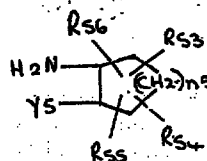
wherein two or three of the dashed lines represent non-allenic double bonds, of which not more than one is outside the N-containing ring; m and n_5 are different integers from one to six, inclusive; and R_{51} , R_{52} , R_{53} , R_{54} , R_{55} , R_{56} , R_{57} and R_{58} are hydrogen or lower alkyl having one to three carbon atoms.

38. A tricyclic pyrazine according to Claim 37 wherein there are three double bonds in the heterocyclic ring; m is one; n_5 is two; R_{51} is a methyl substituent on a carbon atom adjacent to the heterocyclic ring; and R_{52} , R_{53} , R_{54} , R_{55} , R_{56} , R_{57} and R_{58} are hydrogen.

39. A process for the production of a tricyclic pyrazine which comprises reacting a cyclic ketone having the formula



with a cyclic amine having the formula



- to provide a tricyclic dihydropyrazine, wherein m and n , are integers from one to six, inclusive; R_{s1} , R_{s2} , R_{s3} , R_{s4} , R_{s5} , R_{s6} , R_{s7} , and R_{s8} are hydrogen or lower alkyl having one to three carbon atoms; and X_s and Y_s taken together is one of the following pairs of groups:

	X_s	Y_s
	—	—
	(1) carbonyl oxygen	amino
	(2) halo atom	amino
10	(3) amino	halo atom
	(4) amino	carbonyl oxygen;

and dehydrogenating the dihydropyrazine.

40. A process for altering the fragrance of a composition which comprises adding a small but effective amount of at least one pyrazine

material represented by any of the Formulae I, II, III, IVA or IVB herein.

41. A process for the production of a compound according to claim 1, substantially as described in any of the foregoing Examples I—III, V—X, XVII—XIX, XXI—XXVI and XXXIII—XXXV.

42. A compound produced by a process according to claim 8, 15, 16, 17, 18, 19, 24, 25, 26, 33, 34, 39 or 41.

43. A consumable material, composition or article obtained by a process according to claim 2, 7, 14, 23, 32, 35, 36 or 40.

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