

PATENT SPECIFICATION

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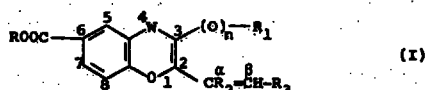


(54) SUBSTITUTED 2-VINYL-CHROMONES

(71) We, CARLO ERBA S.P.A., an Italian Body Corporate of, Via Carlo Imbonati 24, Milan, Italy, do hereby declare the invention for which we pray that a patent may be granted to us, and the method by which it is performed, to be particularly described in and by the following statement:—

The present invention relates to substituted 2-vinyl-chromones, to a process for their preparation and to pharmaceutical compositions containing them.

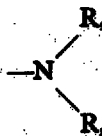
Our co-pending Patent Application No. 24009/77 (Serial No. 1,544,048) relates to compounds having the formula (I)



wherein:

n is zero or 1;

R is hydrogen or C₁—C₁₂ alkyl, unsubstituted or substituted by a C₂—C₃ alkanoyloxy or by a



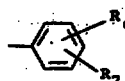
group, wherein each of R₄ and R₅ is independently hydrogen or C₁—C₁₀ alkyl;

R₁ is C₂—C₄ alkyl or C₃—C₄ alkenyl when n is 1, or R₁ is C₃—C₄ alkenyl when n is zero;

R₂ is hydrogen or methyl;

R₃ is (a) a furyl, thienyl or pyridyl which may be unsubstituted or substituted by a methyl group; or

(b) the group

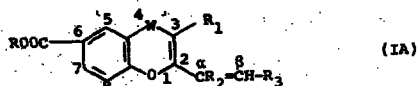


wherein each of R₆ and R₇ is independently (a') hydrogen; (b') halogen; or (c') the group —(O)_n—R₈;

wherein n₁ is zero or 1 and R₈ is C₃—C₄ alkenyl or C₁—C₄ alkyl, the alkenyl and

the alkyl groups being unsubstituted or substituted by one or more C_1-C_2 alkoxy or hydroxy groups;
W is $>C=O$ or $>C=S$.

The present invention provides a compound of formula:



wherein:

R is hydrogen or C_1-C_{12} alkyl, unsubstituted or substituted by a C_2-C_5 alkanoyloxy or by a

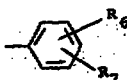


group, wherein each of R_4 and R_5 is independently hydrogen or C_1-C_{10} alkyl;

R_1 is C_2-C_4 alkyl;

R_2 is hydrogen or methyl;

R_3 is (a) a furyl, thienyl or pyridyl group which may be unsubstituted or substituted by a methyl group; or
(b) the group



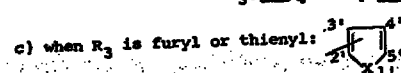
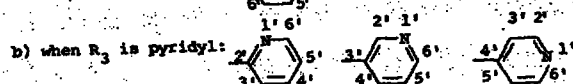
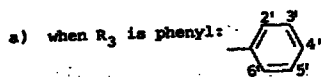
wherein each of R_6 and R_7 is independently (a') hydrogen; (b') halogen or (c') the group $-(O)_{n_1}-R_{60}$, wherein n_1 is zero or 1 and R_{60} is C_2-C_4 alkenyl or

C_1-C_4 alkyl, the alkenyl and the alkyl groups being unsubstituted or substituted by one or more C_1-C_2 alkoxy or hydroxy groups;

W is $>C=O$ or $>C=S$, or, where applicable, a pharmaceutically acceptable salt thereof, as well as all the possible isomers and the mixtures thereof.

In the compounds of the present invention the vinyl moiety may be either in the *cis*- or in the *trans*-configuration, that is the substituent R_3 on the α carbon atom and the hydrogen on the β -carbon atom may be on the same side or on the opposite sides in respect of the vinylic double bond. Also the mixture of the *cis*- and *trans*-isomers is included in the scope of the present invention. Preferably, in the compounds of the invention, the vinyl moiety has the *trans*-configuration.

The numbering used to identify the position of the substituents in the R_3 radical is the conventional one, as is shown by the following examples:



wherein:

X is oxygen or sulphur;

The alkyl, alkenyl, alkoxy and alkanoyloxy groups may be branched or straight chain groups;

When R is an unsubstituted C_1-C_{12} alkyl, it is preferably C_1-C_6 alkyl, in particular methyl, ethyl, isopropyl, t-butyl and hexyl;

When R is a C_1-C_{12} alkyl substituted by C_2-C_5 alkanoyloxy, R is preferably pivaloyloxymethyl;

When R_4 and/or R_5 are C_1-C_{10} alkyl, the alkyl group is preferably C_1-C_4 alkyl, in particular methyl, ethyl, isopropyl and t-butyl;

R_1 is preferably C_2-C_3 alkyl, in particular ethyl and propyl. When R_2 is furyl, thienyl or pyridyl, it is preferably 2-furyl, 2-thienyl or 2-pyridyl.

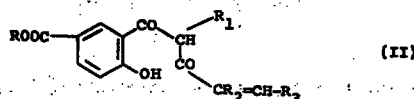
When R_3 is C_1-C_4 alkyl, it is preferably methyl or ethyl. Preferably R_4 and R_5 are independently hydrogen, methoxy, methyl or ethyl. Examples of pharmaceutically acceptable salts are either those with inorganic bases, such as sodium, potassium, calcium and aluminium hydroxides or with organic bases, such as lysine, triethylamine, triethanolamine, dibenzylamine, methylbenzylamine, di-(2-ethyl-hexyl)-amine, piperidine, N-ethyl-piperidine, N,N-diethylaminoethylamine, N-ethylmorpholine, β -phenylethylamine, N-benzyl- β -phenethylamine and N-benzyl-N,N-dimethylamine, as well as the salts with inorganic, e.g. hydrochloric, hydrobromic and sulphuric acids, and with organic acids, e.g. citric, tartaric, maleic, malic, fumaric, methanesulphonic and ethanesulphonic acids. Preferred salts are the sodium and potassium salts, as well as the hydrochlorides of the basic esters, e.g. the diethylaminoethyl and dimethylaminoethyl esters. Particularly preferred compounds of the invention are those of formula (I) wherein R is hydrogen or unsubstituted C_1-C_6 alkyl, R_1 is ethyl or propyl, R_2 is hydrogen or methyl, R_3 is (a) a phenyl group, unsubstituted or substituted by one or two methyl, ethyl or methoxy groups or (b) 2-furyl, 2-thienyl or 2-pyridyl, the furyl, the thienyl and the pyridyl groups being unsubstituted or substituted by a methyl group, and W is $>C=O$ and wherein the vinyl moiety has the *trans*-configuration, as well as their pharmaceutically acceptable salts.

Examples of particularly preferred compounds of the invention are:

- 6 - carboxy - 3 - ethyl - 2 - *trans* - styryl - chromone;
- 6 - carboxy - 3 - propyl - 2 - *trans* - styryl - chromone;
- 6 - carboxy - 3 - propyl - 2 - *trans* - (2' - methyl - styryl) - chromone;
- 6 - carboxy - 3 - propyl - 2 - *trans* - (3' - methyl - styryl) - chromone;
- 6 - carboxy - 3 - propyl - 2 - *trans* - (4' - methyl - styryl) - chromone;
- 6 - carboxy - 3 - propyl - 2 - *trans* - (2',5' - dimethyl - styryl) - chromone;
- 6 - carboxy - 3 - propyl - 2 - *trans* - [β - (2' - thienyl) - vinyl] - chromone;
- 6 - carboxy - 3 - propyl - 2 - *trans* - [β - (2' - furyl - 5' - methyl) - vinyl] - chromone;
- 6 - carboxy - 3 - propyl - 2 - *trans* - [β - (2' - thienyl - 5' - methyl) - vinyl] - chromone;
- 6 - carboxy - 3 - propyl - 2 - *trans* - [β - (2' - pyridyl - 6' - methyl) - vinyl] - chromone;
- 6 - carboxy - 3 - ethyl - 2 - *trans* - [β - (2' - pyridyl - 6' - methyl) - vinyl] - chromone;

as well as the pharmaceutically acceptable base-addition salts thereof, in particular, the sodium salt and the hydrochlorides of the basic esters (e.g. of those with diethylaminoethanol and dimethylaminoethanol) and the C_1-C_6 alkyl esters thereof, in particular the ethyl, isopropyl, t-butyl and hexyl esters. The compounds of the invention are prepared by a process comprising:

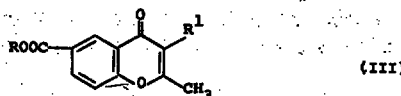
a) cyclising a compound of formula (II)



wherein:

R_1 , R_2 and R_3 are as defined above, so obtaining compounds of formula (IA), wherein W is $>C=O$; or

b) reacting a compound of formula (III)



wherein:

R and R_1 are as defined above, with an aldehyde of formula (IV)



wherein:

R_2 is as defined above, so obtaining compounds of formula (IA) wherein R_2 is hydrogen, W is $>C=O$, and the vinyl moiety has the *trans*-configuration;

and, if desired, converting a resulting compound of formula (IA) wherein W is $>C=O$ into another compound of formula (IA) wherein W is $>C=S$ and/or, if desired, converting a resulting compound of formula (IA) into another compound of formula (IA) by known methods and/or, if desired and applicable, converting a compound of formula (IA) into a pharmaceutically acceptable salt and/or, if desired, converting a salt into a free compound and/or, if desired, separating a mixture of isomers into the single isomers.

The cyclisation of the compound of formula (II) may be preferably performed in the presence of an acid catalyst, such as, for example, hydrochloric acid, hydroiodic acid, sulphuric acid or formic acid, at a temperature ranging preferably between $20^{\circ}C$ and $120^{\circ}C$; the cyclisation reaction is preferably carried out in an inert organic solvent selected, e.g. from methanol, ethanol, dioxane, tetrahydrofuran, benzene, toluene, acetic acid and their mixtures.

The reaction of the compound of formula (III) with the aldehyde of formula (IV) is preferably carried out in the presence of basic condensing agents, such as, for example, sodium ethoxide, sodium methoxide, sodium hydroxide, sodium hydride, sodium amide, in a solvent selected, e.g. from methanol, ethanol, dioxane, water and their mixtures, at a temperature preferably ranging between $0^{\circ}C$ and $120^{\circ}C$.

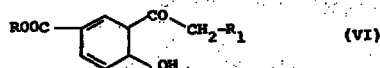
A compound of formula (IA), wherein W is $>C=O$ may be converted into a compound of formula (IA) wherein W is $>C=S$ by reaction, e.g. with P_2S_5 in an inert solvent, such as benzene, toluene, xylene, pyridine at a temperature ranging from the room temperature to $150^{\circ}C$.

A compound of formula (IA) may be converted, as stated above, into another compound of formula (IA) by known methods.

For example, a compound of formula (IA) wherein R is an esterified carboxy group, may be converted into a compound of formula (IA) wherein R is carboxy, by basic hydrolysis, using, e.g., sodium or potassium hydroxide, in a solvent, such as water or a C_1-C_4 aliphatic alcohol, and operating at a temperature ranging from the room temperature to $150^{\circ}C$; the same reaction may also be carried out by treatment with lithium bromide in dimethylformamide at a temperature higher than $50^{\circ}C$. A compound of formula (IA) wherein R is carboxy may be converted into a compound of formula (IA) wherein R is an esterified carboxy group, e.g., a carbalkoxy group, by reaction, for example, of the alkaline salt of the acid with the suitable alkyl halide, in an inert solvent, such as acetone, dioxane, dimethylformamide, hexamethylphosphorotriamide at a temperature ranging from $0^{\circ}C$ to $100^{\circ}C$.

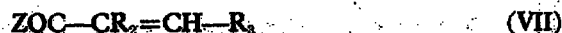
Also the optional salification of a compound of formula (IA) as well as the conversion of a salt into the free compound and the separation of a mixture of isomers into the single isomers may be carried out by conventional methods. For example the separation of a mixture of optical antipodes into the single antipodes may be carried out by salification with an optically active base and by subsequent fractional crystallisation. So the separation of an eventual mixture of *cis*- and *trans*-geometric isomers may be carried out, for example, by fractional crystallisation.

The compound of formula (II) may be prepared by reacting a compound of formula (VI):



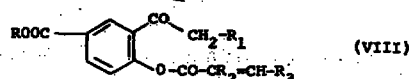
wherein:

R and R_1 are as defined above, with a compound of formula (VII):



wherein:

R_2 , R_3 and Z are as defined above, by conventional methods, e.g., operating in an inert solvent such as benzene, toluene, dioxane at a temperature ranging from $0^{\circ}C$ to the reflux temperature, in the presence of a basic agent, such as pyridine, triethylamine, as acid acceptor, so obtaining a compound of formula (VIII):

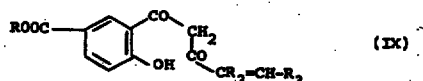


wherein:

R , R_1 , R_2 and R_3 are as defined above and then submitting the compound of formula (VIII) to a rearrangement to give the compounds of formula (II); the rearrangement is carried out in an inert solvent, for example, pyridine,

toluene, methyl ethyl ketone, or isopropyl alcohol, in the presence of a strong base, e.g., sodium, sodium amide, potassium or sodium hydroxide, or potassium carbonate, at a temperature ranging from the room temperature to the reflux temperature.

An alternative method to prepare the compounds of formula (II) is the reaction of a compound of formula (IX)



wherein:

R_1 , R_2 and R_3 are as defined above, with a suitable alkyl or alkenyl halide of formula R_1-Z , wherein R_1 and Z are as defined above, in a solvent such as, for example, dioxane, dimethylformamide, hexamethylphosphorotriamide and their mixtures in the presence of sodium or potassium carbonate, at a temperature ranging from the room temperature to 150°C.

The compounds of formula (III) may be prepared by known methods, for example, by reacting a compound of formula (VI) with an excess of acetic anhydride at a temperature ranging from the room temperature to the reflux temperature, so obtaining compounds of formula (III) wherein n is zero.

The compounds of formula (IV) are commercially available products.

The compounds of formula (VI) may be prepared from the corresponding phenoxy derivatives, which are known compounds, by Fries rearrangement.

The compounds of formula (VII) are known compounds and they may be prepared by conventional methods.

The compounds of formula (IX) may be prepared by reacting the compound of formula (VI) wherein R_1 is hydrogen, with a compound of formula (VII), using the same reaction conditions employed for the preparation of the compound of formula (II).

In the compounds of formula (II), (VII), (VIII) and (IX), the vinyl group may have either the *cis*- or the *trans*-configuration, although it has preferably the *trans*-configuration.

The compounds of the invention have anti-allergic activity, as is shown by the fact that they are active in the passive cutaneous anaphylaxis (PCA) test in rats, according to Goose J. and Blair A.M.J.N. (Immunology, 16, 749, 1969). They can be therefore used in prevention and treatment of bronchial asthma, allergic rhinitis, hay fever, urticaria and dermatosis.

Furthermore, the compounds of the invention offer the important advantage of being highly active as anti-allergic agents also when orally administered, as is shown by the following Table, where the potency ratios of some compounds of the invention are reported with respect to the compound 6 - carboxy - 2 - *trans* - styryl - chromone (K 10210), i.e. the most active compound of the vinylic series described in Belgian Patent 823,875, to the anti-allergic activity of which the conventional value 1 was given.

TABLE

The anti-allergic activity was determined by the inhibition of the IgE-mediated PCA according to Goose J. and Blair A.M.J.N. (*loc. cit.*) using homocytotropic antibodies raised in rats for following the method of Mota I., Immunology, 7, 681 (1964). The tested compounds were administered *per os* 15 minutes before the administration of the antigen at 3 or more dosage levels. At least 8 rats were used per each dose. The potency ratios were calculated according to the method of Finney, D.J. (1952) Statistical Method in Biological Assay, C. Griffin London, page 118.

It is interesting to note that the anti-allergic activity of the compounds of this series is strictly connected with the number of carbon atoms in the R_1 radical. In fact, for instance, the compounds wherein the R_1 radical contains at least two carbon atoms, are much more potent than their lower analogues.

For example the compound 6 - carboxy - 3 - ethyl - 2 - *trans* - styryl - chromone is about 5.5 times more potent than the corresponding 3-methyl derivative and the compound 6 - carboxy - 3 - propyl - 2 - *trans* - chromone is about 7.5 times more potent than the same 3-methyl derivative. Furthermore, the compounds of the invention possess also spasmolytic activity, in particular bronchodilator activity, which is useful in the treatment, for example, of bronchial asthma. The compounds of the invention may be administered in a conventional manner, for instance, orally and

parenterally at a daily dosage preferably of 0.25 to 15 mg/kg, or by inhalation, preferably at a daily dosage of 0.25 to 100 mg, preferably 0.5 to 25 mg, or by topical application.

The nature of the pharmaceutical compositions containing the compounds of this invention in association with pharmaceutically acceptable carriers or diluents will, of course, depend upon the desired mode of administration.

The compositions may be formulated in the conventional manner with the usual ingredients. For example, the compounds of the invention may be administered in the form of aqueous or oily solutions or suspensions, aerosols, as well as powders, tablets, pills, gelatine capsules, syrups, or creams, or lotions for topical use.

Thus, for oral administration, the pharmaceutical compositions containing the compounds of this invention, are preferably tablets, pills or gelatine capsules which contain the active substance together with diluents, such as, for example, lactose, dextrose, sucrose, mannitol, sorbitol, cellulose; lubricants, for instance, silica, talc, stearic acid, magnesium or calcium stearate, and/or polyethylene glycols; or they may also contain binders, such as, for example, starches, gelatine, methylcellulose, carboxymethylcellulose, gum-arabic, tragacanth, polyvinylpyrrolidone, disintegrating agents, such as, for instance, starches, alginic acid, alginates, sodium starch glycolate; effervescent mixtures; dyestuffs; sweeteners; wetting agents, such as, for instance, lecithin, polysorbates, lauryl sulphates; and, in general, non-toxic and pharmacologically inactive substances used in pharmaceutical formulations. Said pharmaceutical preparations may be manufactured in known manner, for example, by means of mixing, granulating, tableting, sugar-coating, or film-coating processes.

For the treatment of allergic asthma, the compounds of the invention are also administered by inhalation. For such use, suitable compositions may comprise a suspension or solution of the active ingredient, preferably in the form of a salt, such as the sodium salt, in water, for administration by means of a conventional nebuliser. Alternatively, the compositions may comprise a suspension or a solution of the active ingredient in a conventional liquified propellant, such as, dichlorodifluoromethane or dichlorotetrafluoroethane to be administered from a pressurised container, i.e., an aerosol dispenser. When the medicament is not soluble in the propellant, it may be necessary to add a co-solvent, such as, ethanol, dipropylene glycol, isopropyl myristate, and/or a surface-active agent to the composition, in order to suspend the medicament in the propellant medium and such surface-active agents may be any of those commonly used for this purpose, such as non-ionic surface-active agents, e.g., lecithin. The compounds of the invention may also be administered in the form of powders by means of a suitable insufflator device and in this case the fine particle sized powders of the active ingredient may be mixed with a diluent material such as lactose.

Furthermore, the compounds of this invention may also be administered by intradermal or intravenous injection in the conventional manner.

In addition to the internal administration, the compounds of this invention may find use in compositions for topical application, e.g. as creams, lotions or pastes for use in dermatological treatments. For these compositions the active ingredient may be mixed with conventional oleaginous or emulsifying excipients.

The following examples illustrate but do not limit the present invention.

EXAMPLE 1

14 Grams of methyl 3 - butyryl - 4 - hydroxy - benzoate (m.p.=54-55°C) dissolved in dioxane (80 ml) containing pyridine (20 ml) were reacted with trans-cinnamoyl chloride at room temperature for 20 hours. The reaction mixture was diluted with water, acidified to pH 4 with 23% HCl and extracted with ethyl acetate. The separated organic phase was washed with 5% NaHCO₃ and water and then evaporated to dryness. The obtained residue (24 g) was dissolved in methyl - ethyl-ketone (240 ml), anhydrous K₂CO₃ (62 g) was added and the mixture was vigorously stirred under reflux for 3 hours.

After cooling the mixture was diluted with cyclohexane (250 ml) and filtered. The collected product was dissolved in water and precipitated by the addition of an excess of 20% citric acid.

After filtration, washing with water and drying, crude 1 - (2 - hydroxy - 5 - carbomethoxy - benzoyl) - 1 - trans - cinnamoyl - propane (17.8 g) was obtained, which was dissolved in 99% formic acid (50 ml) and heated under reflux for 20 minutes. After cooling the mixture was diluted with ice-water and filtered. After crystallisation from ethanol, 6 - carbomethoxy - 3 - ethyl - 2 - trans - styryl - chromone (9.7 g), m.p.=194-195°C, NMR (CF₃COOD): vinylic protons δ_{HB} =7.49(d), δ_{Ha} =8.31(d), p.p.m., J_{HaHB} =15.5 Hz, was obtained and treated with 1% KOH solution (190 ml) in 95%

ethanol under reflux for 30 minutes. After cooling, the mixture was acidified with 23% HCl to pH 4 and the precipitate was filtered, washed with ethanol and water until neutral so obtaining 6 - carboxy - 3 - ethyl - 2 - *trans* - styryl - chromone (8.4 g), m.p.=282—284°C; IR: δ (C—H) $\gt$ C=C $\lt$ (*trans*) 960 cm⁻¹; NMR (CF₃COOD): vinylic protons $\delta_{H\beta}$ =7.43(d), δ_{Ha} =8.16(d) p.p.m., $J_{HaH\beta}$ =15.5 Hz.

By proceeding analogously and starting from suitable intermediates, the following compounds were obtained:

6 - carboxy - 3 - propyl - 2 - *trans* - styryl - chromone, m.p.=270—272°C, IR: δ (C—H) $\gt$ C=C $\lt$ (*trans*) 995 cm⁻¹; NMR (CF₃COOD): vinylic proton $\delta_{H\beta}$ =7.52(d), δ_{Ha} =8.27(d), p.p.m., $J_{HaH\beta}$ =15.9 Hz;

6 - carboxy - 3 - isopropyl - 2 - *trans* - styryl - chromone, m.p.=271—273°C, IR: δ (C—H) $\gt$ C=C $\lt$ (*trans*) 960 cm⁻¹; NMR (CF₃COOD): vinylic protons $\delta_{H\beta}$ =7.24(d), δ_{Ha} =7.64(d) p.p.m., $J_{HaH\beta}$ =16 Hz;

6 - carboxy - 3 - butyl - 2 - *trans* - styryl - chromone, m.p.=261—262°C, IR: δ (C—H) $\gt$ C=C $\lt$ (*trans*) 955 cm⁻¹;

6 - carboxy - 3 - ethyl - 2 - *trans* - (2' - methyl - styryl) - chromone, m.p.=270—271°C; NMR (CF₃COOD): vinylic protons $\delta_{H\beta}$ =7.27(d), δ_{Ha} =8.38(d) p.p.m., $J_{HaH\beta}$ =16 Hz; IR δ (C—H) $\gt$ C=C $\lt$ (*trans*) 960 cm⁻¹;

6 - carboxy - 3 - ethyl - 2 - *trans* - (2' - ethyl - styryl) - chromone; 6 - carboxy - 3 - butyl - 2 - *trans* - (2' - methyl - styryl) - chromone; 6 - carboxy - 3 - propyl - 2 - *trans* (2' - methyl - styryl) chromone, m.p.=234—237°C; NMR (CF₃COOD): vinylic protons $\delta_{H\beta}$ =7.34(d), δ_{Ha} =8.53(d) p.p.m., $J_{HaH\beta}$ =16 Hz; IR: δ (C—H) $\gt$ C=C $\lt$ (*trans*) 960 cm⁻¹;

6 - carboxy - 3 - propyl - 2 - *trans* - (4' - methyl - styryl) - chromone, m.p.=266—267°C;

6 - carboxy - 3 - propyl - 2 - *trans* - (3' - methyl - styryl) - chromone, m.p.=246—247°C; IR (KBr): δ (C—H) $\gt$ C=C $\lt$ (*trans*) 960 cm⁻¹;

6 - carboxy - 3 - ethyl - 2 - *cis* - styryl - chromone;

6 - carboxy - 3 - propyl - 2 - *cis* - styryl chromone;

6 - carboxy - 3 - propyl - 2 - *cis* - (2' - methyl - styryl) - chromone.

EXAMPLE 2

By proceeding according to Example 1 and starting from the suitable α - methyl - *trans* - cinnamoyl - chlorides, the following compounds were prepared:

6 - carboxy - 3 - ethyl - 2 - *trans* - (α - methyl - styryl) - chromone, m.p.=193—194°C; NMR (CF₃COOD): vinylic proton $\delta_{H\beta}$ =7.13 p.p.m., J (allylic constant)=1.5 Hz;

6 - carboxy - 3 - propyl - 2 - *trans* - (α - methyl - styryl) - chromone, m.p.=176—178°C;

6 - carboxy - 3 - ethyl - 2 - *trans*(α ,2' - dimethyl - styryl) - chromone;

6 - carboxy - 3 - propyl - 2 - *trans*(α ,2' - dimethyl - styryl) - chromone, m.p.=173—174°C.

EXAMPLE 3

64 Grams of methyl 3 - valeroyl - 4 - hydroxybenzoate (m.p.=78—80°C) were reacted with acetic anhydride (138 ml) in the presence of triethylamine (38 ml) under reflux for 4 hours. After cooling the reaction mixture was diluted with water and ice. The aqueous phase was decanted and the thick oily precipitate was extracted with ethyl acetate. The organic phase was washed with 5% NaHCO₃ and water and then evaporated to dryness. The residue, 69.2 g of crude 6 - carbomethoxy - 3 - propyl - 2 - methyl - chromone, was dissolved in anhydrous methanol (300 ml) and benzaldehyde (58 ml) and the solution was slowly added to a solution of sodium (12.4 g) in anhydrous methanol (250 ml).

After 20 hours at room temperature, the precipitate was filtered and washed with methanol and water to obtain 32.5 g of 6 - carbomethoxy - 3 - propyl - 2 - *trans* - styryl - chromone, m.p.=210—212°C, which were treated with a 1% KOH solution (600 ml) in 95% ethanol under reflux for 30 minutes. After cooling the mixture was acidified with 23% HCl to pH=4, the precipitate was filtered, washed with ethanol and then with water until neutral so obtaining 6 - carboxy - 3 - propyl - 2 - *trans* - styryl - chromone (28 g), m.p.=210—212°C, IR: δ (C—H) $\gt$ C=C $\lt$ (*trans*) 955 cm⁻¹; NMR (CF₃COOD): vinylic protons $\delta_{H\beta}$ =7.52(d), δ_{Ha} =8.27(d) p.p.m., $J_{HaH\beta}$ =15.9 Hz.

By proceeding analogously and starting from the suitable substituted benzaldehydes the following compounds were prepared:

6 - carboxy - 3 - propyl - 2 - *trans*(2' - methyl - styryl) - chromone, m.p.=234—237°C, IR: (C—H) $\gt$ C=C $\lt$ (*trans*) 960 cm⁻¹; NMR (CF₃COOD): vinylic protons $\delta_{H\beta}$ =7.34(d), δ_{Ha} =8.53(d) p.p.m., $J_{HaH\beta}$ =16 Hz;

6 - carboxy - 3 - propyl - 2 - *trans* - (3' - methyl - styryl) - chromone, m.p.=
246—247°C, IR (KBr): $\delta(\text{C—H}) > \text{C}=\text{C} < (\text{trans})$ 960 cm^{-1} ; NMR (CF_3COOD):
vinylc protons $\delta_{\text{H}\beta}=7.54(\text{d})$, $\delta_{\text{H}\alpha}=8.36(\text{d})$ p.p.m., $J_{\text{H}\alpha\text{H}\beta}=16$ Hz;

6 - carboxy - 3 - propyl - 2 - *trans* - (4' - methyl - styryl) - chromone, m.p.=
266—267°C;

6 - carboxy - 3 - propyl - 2 - *trans* - (2' - ethyl - styryl) - chromone, m.p.=
232—233°C;

6 - carboxy - 3 - propyl - 2 - *trans* - (2' - methoxy - styryl) - chromone, m.p.=
263—264°C, IR: $\delta(\text{C—H}) > \text{C}=\text{C} < (\text{trans})$ 965 cm^{-1} ; NMR (CF_3COOD): vinylc
protons $\delta_{\text{H}\beta}=7.67(\text{d})$, $\delta_{\text{H}\alpha}=8.4(\text{d})$ p.p.m., $J_{\text{H}\alpha\text{H}\beta}=16$ Hz;

6 - carboxy - 3 - propyl - 2 - *trans* - (2' - ethoxy - styryl) - chromone, m.p.=
270—271°C, IR: $\delta(\text{C—H}) > \text{C}=\text{C} < (\text{trans})$ 960 cm^{-1} ; NMR (CF_3COOD): vinylc
protons $\delta_{\text{H}\beta}=8.00(\text{d})$, $\delta_{\text{H}\alpha}=8.50(\text{d})$ p.p.m., $J_{\text{H}\alpha\text{H}\beta}=16$ Hz;

6 - carboxy - 3 - propyl - 2 - *trans* - (3' - methoxy - styryl) - chromone, m.p.=
231—232°C, IR: $\delta(\text{C—H}) > \text{C}=\text{C} < (\text{trans})$ 950 cm^{-1} ; NMR (CF_3COOD): vinylc
protons $\delta_{\text{H}\beta}=7.33(\text{d})$, $\delta_{\text{H}\alpha}=7.86(\text{d})$ p.p.m., $J_{\text{H}\alpha\text{H}\beta}=15.5$ Hz;

6 - carboxy - 3 - propyl - 2 - *trans* - (4' - methoxy - styryl) - chromone;

6 - carboxy - 3 - propyl - 2 - *trans* - (2',5' - dimethyl - styryl) - chromone;

6 - carboxy - 3 - propyl - 2 - *trans* - (2' - fluoro - styryl) - chromone, m.p.=
254—255°C, IR: $\delta(\text{C—H}) > \text{C}=\text{C} < (\text{trans})$ 970, 960 cm^{-1} ; NMR (CF_3COOD):
vinylc protons $\delta_{\text{H}\beta}=7.84(\text{d})$, $\delta_{\text{H}\alpha}=8.62(\text{d})$ p.p.m., $J_{\text{H}\alpha\text{H}\beta}=16$ Hz;

6 - carboxy - 3 - propyl - 2 - *trans* - (4' - fluoro - styryl) - chromone, m.p.=
295—297°C, IR: $\delta(\text{C—H}) > \text{C}=\text{C} < (\text{trans})$ 960 cm^{-1} ; NMR (CF_3COOD):
vinylc protons $\delta_{\text{H}\beta}=7.44(\text{d})$, $\delta_{\text{H}\alpha}=8.27(\text{d})$ p.p.m., $J_{\text{H}\alpha\text{H}\beta}=16$ Hz.

EXAMPLE 4

By proceeding according to Example 3 and starting from methyl 3 - butyryl - 4 -
hydroxy - benzoate, the following compounds were prepared:

6 - carboxy - 3 - ethyl - 2 - *trans* - styryl - chromone, m.p.=282—284°C, IR:
 $\delta(\text{C—H}) > \text{C}=\text{C} < (\text{trans})$ 960 cm^{-1} ; NMR (CF_3COOD): vinylc protons $\delta_{\text{H}\beta}=7.43(\text{d})$,
 $\delta_{\text{H}\alpha}=8.16(\text{d})$ p.p.m., $J_{\text{H}\alpha\text{H}\beta}=15.5$ Hz;

6 - carboxy - 3 - ethyl - 2 - *trans* - (2' - methyl - styryl) - chromone, m.p.=
270—271°C, IR: $\delta(\text{C—H}) > \text{C}=\text{C} < (\text{trans})$ 960 cm^{-1} ; NMR (CF_3COOD): vinylc
protons $\delta_{\text{H}\beta}=7.27(\text{d})$, $\delta_{\text{H}\alpha}=8.38(\text{d})$ p.p.m., $J_{\text{H}\alpha\text{H}\beta}=16$ Hz;

6 - carboxy - 3 - ethyl - 2 - *trans* - (3' - methyl - styryl) - chromone;

6 - carboxy - 3 - ethyl - 2 - *trans* - (4' - methyl - styryl) - chromone;

6 - carboxy - 3 - ethyl - 2 - *trans* - (2' - ethyl - styryl) - chromone;

6 - carboxy - 3 - ethyl - 2 - *trans* - (2' - methoxy - styryl) - chromone, m.p.=
280—281°C, IR: $\delta(\text{C—H}) > \text{C}=\text{C} < (\text{trans})$ 970 cm^{-1} ; NMR (CF_3COOD): vinylc
protons $\delta_{\text{H}\beta}=7.81(\text{d})$, $\delta_{\text{H}\alpha}=8.69(\text{d})$ p.p.m., $J_{\text{H}\alpha\text{H}\beta}=15.5$ Hz;

6 - carboxy - 3 - ethyl - 2 - *trans* - [2' - (2 - ethoxyethoxy) - styryl] - chromone,
m.p.=225—227°C, IR: $\delta(\text{C—H}) > \text{C}=\text{C} < (\text{trans})$ 955 cm^{-1} ; NMR (CF_3COOD):
vinylc protons $\delta_{\text{H}\beta}=7.62(\text{d})$, $\delta_{\text{H}\alpha}=8.55(\text{d})$ p.p.m., $J_{\text{H}\alpha\text{H}\beta}=16$ Hz;

6 - carboxy - 3 - ethyl - 2 - *trans* - 2',5' - dimethyl - styryl - chromone.

EXAMPLE 5

By proceeding according to Examples 3 and 4 and using the suitable heterocyclic
aldehydes, the following compounds were obtained:

6 - carboxy - 3 - ethyl - 2 - *trans* - [β - (2' - thienyl - 5' - methyl) - vinyl] -
chromone;

6 - carboxy - 3 - ethyl - 2 - *trans* - [β - (2' - furyl - 5' - methyl) - vinyl] -
chromone;

6 - carboxy - 3 - ethyl - 2 - *trans* - [β - (2' - pyridyl - 6' - methyl) - vinyl] -
chromone;

6 - carboxy - 3 - ethyl - 2 - *trans* - [β - (2' - thienyl) - vinyl] - chromone, m.p.
=268—270°C, IR: $\delta(\text{C—H}) > \text{C}=\text{C} < (\text{trans})$ 960 cm^{-1} ; NMR ($\text{DMSO}-d_6$ - CDCl_3
50:50): vinylc protons $\delta_{\text{H}\beta}=6.98(\text{d})$, $\delta_{\text{H}\alpha}=7.88(\text{d})$ p.p.m., $J_{\text{H}\alpha\text{H}\beta}=15.5$ Hz;

6 - carboxy - 3 - ethyl - 2 - *trans* - [β - (2' - pyridyl) - vinyl] - chromone, m.p.
=283—286°C, IR (KBr): $\delta(\text{C—H}) > \text{C}=\text{C} < (\text{trans})$ 960 cm^{-1} ; NMR (CF_3COOD):
vinylc protons $\delta_{\text{H}\alpha+\text{H}\beta}=7.99$ (s);

6 - carboxy - 3 - propyl - 2 - *trans* - [β - (2' - furyl) - vinyl] - chromone, m.p.
=220—222°C, IR (KBr): $\delta(\text{C—H}) > \text{C}=\text{C} < (\text{trans})$ 955 cm^{-1} ; NMR
(CF_3COOD): vinylc protons $\delta_{\text{H}\beta}=7.38(\text{d})$, $\delta_{\text{H}\alpha}=8.14(\text{d})$ p.p.m., $J_{\text{H}\alpha\text{H}\beta}=15$ Hz;

6 - carboxy - 3 - propyl - 2 - *trans* - [β - (2' - thienyl) - vinyl] - chromone, m.p.

=243—245°C, IR: δ (C—H) $\gt$ C=C $\lt$ (trans) 940 cm⁻¹; NMR (CF₃COOD): vinylic protons $\delta_{H\beta}$ =7.24(d), $\delta_{H\alpha}$ =8.51(d) p.p.m., $J_{H\alpha H\beta}$ =15 Hz;

6 - carboxy - 3 - propyl - 2 - trans - [β - (2' - pyridyl) - vinyl] - chromone, m.p.=278—280°C, IR: δ (C—H) $\gt$ C=C $\lt$ (trans) 955 cm⁻¹; NMR (CF₃COOD): protons $\delta_{H\alpha+H\beta}$ =7.99 (s);

6 - carboxy - 3 - propyl - 2 - trans - [β - (3' - pyridyl) - vinyl] - chromone, m.p.=308—309°C; IR: δ (C—H) $\gt$ C=C $\lt$ (trans) 960 cm⁻¹; NMR (CF₃COOD): vinylic protons $\delta_{H\beta}$ =7.74(d), $\delta_{H\alpha}$ =8.06(d) p.p.m., $J_{H\alpha H\beta}$ =16 Hz;

6 - carboxy - 3 - propyl - 2 - trans - [β - (2' - furyl - 5' - methyl) - vinyl] - chromone, m.p.=244—247°C; IR (KBr): δ (C—H) $\gt$ C=C $\lt$ (trans) 950 cm⁻¹; NMR (CF₃COOD): vinylic protons $\delta_{H\beta}$ =7.32(d), $\delta_{H\alpha}$ =8.18(d) p.p.m., $J_{H\alpha H\beta}$ =16 Hz;

6 - carboxy - 3 - propyl - 2 - trans - [β - (2' - pyridyl - 6' - methyl) - vinyl] - chromone;

6 - carboxy - 3 - propyl - 2 - trans - [β - (2' - thienyl - 5' - methyl) - vinyl] - chromone.

EXAMPLE 6

12 Grams of 6 - carboxy - 3 - propyl - 2 - trans - styryl - chromone were reactedd with thionyl chloride (4 ml) in dichloroethane (80 ml) at the reflux temperature for 2 hours. After cooling, the reaction mixture was evaporated to dryness and reacted with an excess of anhydrous ethanol at 50°C for 1 hour. The mixture was concentrated at small volume and diluted with water to obtain, by filtration, 6 - carbomethoxy - 3 - propyl - 2 - trans - styryl - chromone (9.6 g), m.p.=154—156°C, IR: δ (C—H) $\gt$ C=C $\lt$ (trans) 960 cm⁻¹; NMR (CDCl₃): vinylic protons $\delta_{H\beta}$ =7.07(d), $\delta_{H\alpha}$ =7.58(d) p.p.m., $J_{H\alpha H\beta}$ =16 Hz.

By preceding analogously the following compounds were prepared:

6 - carbethoxy - 3 - propyl - 2 - trans - (2' - methyl - styryl) - chromone;

6 - carbethoxy - 3 - propyl - 2 - trans - (3' - methyl - styryl) - chromone;

6 - carbethoxy - 3 - propyl - 2 - trans - (4' - methyl - styryl) - chromone;

6 - carbethoxy - 3 - propyl - 2 - trans - (2',5' - dimethyl - styryl) - chromone;

6 - carbethoxy - 3 - propyl - 2 - trans - [β - (2' - furyl - 5' - methyl) - vinyl] - chromone;

6 - carbethoxy - 3 - propyl - 2 - trans - [β - (2' - thienyl) - vinyl] - chromone;

6 - carbethoxy - 3 - propyl - 2 - trans - [β - (2' - pyridyl - 6' - methyl) - vinyl] - chromone;

6 - carbethoxy - 3 - ethyl - 2 - trans - styryl - chromone;

6 - carbethoxy - 3 - ethyl - 2 - trans - [β - (2',5' - methyl) - vinyl] - chromone;

6 - carbethoxy - 3 - propyl - 2 - cis - (2' - methyl - styryl) - chromone;

6 - carbethoxy - 3 - propyl - 2 - cis - styryl - chromone;

6 - carbethoxy - 3 - ethyl - 2 - cis - styryl - chromone.

EXAMPLE 7

By proceeding according to Example 6 and using the suitable aliphatic alcohols the isopropyl ester, t-butyl ester, hexyl ester, octyl ester and undecyl ester of the following acids were prepared:

6 - carboxy - 3 - propyl - 2 - trans - styryl - chromone;

6 - carboxy - 3 - propyl - 2 - trans - (2' - methyl - styryl) - chromone;

6 - carboxy - 3 - propyl - 2 - trans - (3' - methyl - styryl) - chromone;

6 - carboxy - 3 - propyl - 2 - trans - (4' - methyl - styryl) - chromone;

6 - carboxy - 3 - propyl - 2 - trans - 2',5' - dimethyl - styryl - chromone;

6 - carboxy - 3 - propyl - 2 - trans - [β - (2' - furyl - 5 - methyl) - vinyl] - chromone;

6 - carboxy - 3 - propyl - 2 - trans - [β - (2' - thienyl) - vinyl] chromone;

6 - carboxy - 3 - propyl - 2 - trans - [β - (2' - thienyl - 5' - methyl) - vinyl] - chromone;

6 - carboxy - 3 - propyl - 2 - trans - [β - (2' - pyridyl - 6' - methyl) - vinyl] - chromone;

6 - carboxy - 3 - ethyl - 2 - trans - styryl - chromone;

6 - carboxy - 3 - ethyl - 2 - trans - [β - (2' - pyridyl) - vinyl] - chromone;

6 - carboxy - 3 - ethyl - 2 - trans - [β - (2' - pyridyl - 6' - methyl) - vinyl] - chromone.

EXAMPLE 8

5 Grams of 6 - carboxy - 3 - propyl - 2 - trans - (2' - methyl - styryl) - chromone were reactedd at 100°C with NaHCO₃ (1.25 g) in water (25 ml), working far from the light, until the solution is completed. By cooling the solution to 5°C, a precipitate

was obtained, which was then filtered and washed with icy water to give the sodium salt of 6 - carboxy - 3 - propyl - 2 - *trans* - (2' - methyl - styryl) - chromone (4.4 g).

By proceeding analogously the sodium salts of the following acids were prepared:

- 6 - carboxy - 3 - propyl - 2 - *cis* - styryl - chromone;
- 6 - carboxy - 3 - ethyl - 2 - *cis* - styryl - chromone;
- 6 - carboxy - 3 - propyl - 2 - *cis* - (2' - methyl - styryl) - chromone;
- 6 - carboxy - 3 - propyl - 2 - *trans* - styryl - chromone;
- 6 - carboxy - 3 - ethyl - 2 - *trans* - styryl - chromone;
- 6 - carboxy - 3 - propyl - 2 - *trans* - (3' - methyl - styryl) - chromone;
- 6 - carboxy - 3 - propyl - 2 - *trans* - [β - (2' - thienyl) - vinyl] - chromone;
- 6 - carboxy - 3 - propyl - 2 - *trans* - [β - (2' - furyl - 5' - methyl - vinyl) - chromone;
- 6 - carboxy - 3 - propyl - 2 - *trans* - [β - (2' - pyridyl - 6 - methyl) - vinyl] - chromone;
- 6 - carboxy - 3 - propyl - 2 - *trans* - (4' - methyl - styryl) - chromone;
- 6 - carboxy - 3 - propyl - 2 - *trans* - (2',5' - dimethyl - styryl) - chromone;
- 6 - carboxy - 3 - ethyl - 2 - *trans* - [β - (2' - furyl - 5' - methyl) - vinyl] - chromone;

EXAMPLE 9

A mixture of 3.5 g of 6 - carboxy - 3 - propyl - 2 - *trans* - (2' - methyl - styryl) - chromone and N - methyl - N - benzylamine (1.6 g) was stirred at 120°C for 30 minutes. After cooling, ethyl acetate (50 ml) was added and the mixture was left to crystallise under stirring. After filtration and washing with ethyl acetate 4.1 g of the N - methyl - N - benzylammonium salt of 6 - carboxy - 3 - propyl - 2 - *trans* - (2' - methyl - styryl) - chromone were obtained.

By proceeding analogously the N - methyl - N - benzyl - ammonium salts of the acids listed in Example 13 were prepared.

EXAMPLE 10

6.2 Grams of 3 - propyl - 2 - *trans* - styryl - chromone - 6 - carbonyl - chloride prepared according to Example 6 were dissolved in dioxane (40 ml) and reacted with 2 - diethylamino - ethanol (2 ml) in the presence of triethylamine (1 ml) at room temperature for 20 hours. The reaction mixture was diluted with water and filtered. The collected product was dissolved in acetone (200 ml) and treated with the stoichiometric amount of concentrated HCl. The so obtained precipitate was filtered, washed with acetone and dissolved in water. After alkalisation of the aqueous solution with K_2CO_3 and filtration the diethylaminoethyl ester (4.5 g) of the 6 - carboxy - 3 - propyl - 2 - *trans* - styryl - chromone, m.p.=89-91°C, IR: δ (C-H) > C=C < (*trans*) 960 cm^{-1} ; NMR ($CDCl_3$): vinylic protons $\delta_{H\beta}$ =7.10(d), δ_{Ha} =7.62(d) p.p.m., $J_{Ha\beta}$ =16 Hz was obtained.

Analogously the diethylaminoethyl esters of the following acids were prepared:

- 6 - carboxy - 3 - propyl - 2 - *trans* - (2',5' - dimethyl - styryl) - chromone;
- 6 - carboxy - 3 - propyl - 2 - *trans* - (4' - methyl - styryl) - chromone;
- 6 - carboxy - 3 - propyl - 2 - *trans* - (2' - methyl - styryl) - chromone;
- 6 - carboxy - 3 - propyl - 2 - *trans* - (3' - methyl - styryl) - chromone;
- 6 - carboxy - 3 - propyl - 2 - *trans* - [β - (2' - furyl - 5' - methyl) - vinyl] - chromone;
- 6 - carboxy - 3 - propyl - 2 - *trans* - [β - (2' - thienyl - 5' - methyl) - vinyl] - chromone;
- 6 - carboxy - 3 - propyl - 2 - *trans* - [β - (2' - thienyl) - vinyl] - chromone;
- 6 - carboxy - 3 - ethyl - 2 - *trans* - styryl - chromone;
- 6 - carboxy - 3 - propyl - 2 - *trans* - [β - (2' - thienyl - 5' - methyl) - vinyl] - chromone;
- 6 - carboxy - 3 - ethyl - 2 - *cis* - styryl - chromone;
- 6 - carboxy - 3 - propyl - 2 - *cis* - styryl - chromone;
- 6 - carboxy - 3 - propyl - 2 - *cis* - (2' - methyl - styryl) - chromone.

EXAMPLE 11

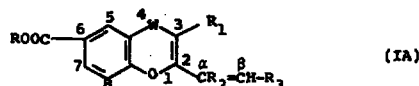
5 Grams of 6 - carboxy - 3 - propyl - 2 - *trans* - styryl - chromone, obtained proceeding according to Example 6, were reacted with P_2S_5 (3.9 g) in dioxane (100 ml) at the reflux temperature for 3 hours. After cooling, 1N NaOH (75 ml) was cautiously added. The mixture was stirred for 1 hour at room temperature, far from the light, acidified with 2N HCl and filtered. After crystallisation from ethyl acetate 6 - carboxy - 3 - propyl - 2 - *trans* - styryl - 4 - thio - chromone (2.7 g) was obtained.

By proceeding analogously, the following compounds were prepared:

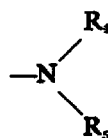
- 6 - carboxy - 3 - propyl - 2 - *trans* - (2' - methyl - styryl) - 4 - thio - chromone;
 6 - carboxy - 3 - propyl - 2 - *trans* - (3 - methyl - styryl) - 4 - thio - chromone;
 6 - carboxy - 3 - ethyl - 2 - *trans* - styryl - 4 - thio - chromone;
 6 - carboxy - 3 - propyl - 2 - *trans* - (3' - methyl - styryl) - 4 - thio - chromone;
 5 chromone;
 6 - carboxy - 3 - propyl - 2 - *trans* - (2',5' - dimethyl - styryl) - chromone;
 6 - carboxy - 3 - ethyl - 2 - *cis* - styryl - 4 - thio - chromone;
 6 - carboxy - 3 - propyl - 2 - *cis* - styryl - 4 - thio - chromone.
 10 The invention includes a method of treating an allergy in a warm-blooded non-human animal, comprising administering thereto a therapeutically effective dose of a compound according to the invention. 10

WHAT WE CLAIM IS:—

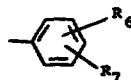
1. A compound of formula:



- 15 wherein R is hydrogen or C₁—C₁₂ alkyl, unsubstituted or substituted by a C₂—C₅ alkanoyloxy or by a 15



- group, wherein each of R₄ and R₅ is independently hydrogen or C₁—C₁₀ alkyl;
 20 R₁ is C₂—C₄ alkyl;
 R₂ is hydrogen or methyl;
 R₃ is (a) a furyl, thienyl or pyridyl group which may be unsubstituted or substituted by a methyl group; or (b) the group 20



- 25 wherein each of R₆ and R₇ is independently (a') hydrogen; (b') halogen or (c') the group —(O)_n—R₈, wherein n₁ is zero or 1 and R₈ is C₃—C₄ alkenyl 25
 alkenyl or C₁—C₄ alkyl, the alkenyl and the alkyl groups being unsubstituted or substituted by one or more C₁—C₂ alkoxy or hydroxy groups; W is
 30 > C=O or > C=S, or, where applicable, a pharmaceutically acceptable salt thereof. 30

2. 6 - Carboxy - 3 - ethyl - 2 - *trans* - styryl - chromone.
 3. 6 - Carboxy - 3 - propyl - 2 - *trans* - styryl - chromone.
 4. 6 - Carboxy - 3 - propyl - 2 - *trans* - (2' - methyl - styryl) - chromone.
 5. 6 - Carboxy - 3 - propyl - 2 - *trans* - (3' - methyl - styryl) - chromone.
 35 6. 6 - Carboxy - 3 - propyl - 2 - *trans* - (4' - methyl - styryl) - chromone. 35
 7. 6 - Carboxy - 3 - propyl - 2 - *trans* - (2',5' - dimethyl - styryl) - chromone.
 8. 6 - Carboxy - 3 - propyl - 2 - *trans* - [β - (2' - thienyl) - vinyl] - chromone.
 9. 6 - Carboxy - 3 - propyl - 2 - *trans* - [β - (2' - furyl - 5' - methyl) - vinyl] - chromone.
 40 10. 6 - Carboxy - 3 - propyl - 2 - *trans* - [β - (2' - thienyl - 5' - methyl) - vinyl] - chromone. 40
 11. 6 - Carboxy - 3 - propyl - 2 - *trans* - [β - (2' - pyridyl - 6' - methyl) - vinyl] - chromone.
 12. 6 - Carboxy - 3 - ethyl - 2 - *trans* - [β - (2' - pyridyl - 6' - methyl) - vinyl] - chromone.
 45 13. Any one of the compounds according to claim 1 hereinbefore specifically disclosed, except those according to claims 2 to 12. 45
 14. A pharmaceutically acceptable base addition salt of a compound according to any one of claims 2 to 12.



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6 - carboxy - 3 - propyl - 2 - *trans* - (2' - methyl - styryl) - 4 - thio - chromone;
 6 - carboxy - 3 - propyl - 2 - *trans* - (3 - methyl - styryl) - 4 - thio - chromone;
 6 - carboxy - 3 - ethyl - 2 - *trans* - styryl - 4 - thio - chromone;
 6 - carboxy - 3 - propyl - 2 - *trans* - (3' - methyl - styryl) - 4 - thio - chromone;

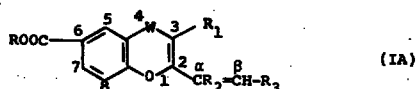
chromone;

6 - carboxy - 3 - propyl - 2 - *trans* - (2',5' - dimethyl - styryl) - chromone;
 6 - carboxy - 3 - ethyl - 2 - *cis* - styryl - 4 - thio - chromone;
 6 - carboxy - 3 - propyl - 2 - *cis* - styryl - 4 - thio - chromone.

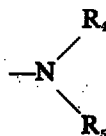
The invention includes a method of treating an allergy in a warm-blooded non-human animal, comprising administering thereto a therapeutically effective dose of a compound according to the invention.

WHAT WE CLAIM IS:—

1. A compound of formula:



wherein R is hydrogen or C₁—C₁₂ alkyl, unsubstituted or substituted by a C₂—C₅ alkanoyloxy or by a

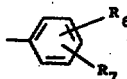


group, wherein each of R₄ and R₅ is independently hydrogen or C₁—C₁₀ alkyl;

R₁ is C₂—C₄ alkyl;

R₂ is hydrogen or methyl;

R₃ is (a) a furyl, thienyl or pyridyl group which may be unsubstituted or substituted by a methyl group; or (b) the group



wherein each of R₆ and R₇ is independently (a') hydrogen; (b') halogen or (c') the group —(O)_n—R₈, wherein n₁ is zero or 1 and R₈ is C₃—C₄ alkenyl

alkenyl or C₁—C₄ alkyl, the alkenyl and the alkyl groups being unsubstituted or substituted by one or more C₁—C₂ alkoxy or hydroxy groups; W is > C=O or > C=S, or, where applicable, a pharmaceutically acceptable salt thereof.

2. 6 - Carboxy - 3 - ethyl - 2 - *trans* - styryl - chromone.

3. 6 - Carboxy - 3 - propyl - 2 - *trans* - styryl - chromone.

4. 6 - Carboxy - 3 - propyl - 2 - *trans* - (2' - methyl - styryl) - chromone.

5. 6 - Carboxy - 3 - propyl - 2 - *trans* - (3' - methyl - styryl) - chromone.

6. 6 - Carboxy - 3 - propyl - 2 - *trans* - (4' - methyl - styryl) - chromone.

7. 6 - Carboxy - 3 - propyl - 2 - *trans* - (2',5' - dimethyl - styryl) - chromone.

8. 6 - Carboxy - 3 - propyl - 2 - *trans* - [β - (2' - thienyl) - vinyl] - chromone.

9. 6 - Carboxy - 3 - propyl - 2 - *trans* - [β - (2' - furyl - 5' - methyl) - vinyl] - chromone.

10. 6 - Carboxy - 3 - propyl - 2 - *trans* - [β - (2' - thienyl - 5' - methyl) - vinyl] - chromone.

11. 6 - Carboxy - 3 - propyl - 2 - *trans* - [β - (2' - pyridyl - 6' - methyl) - vinyl] - chromone.

12. 6 - Carboxy - 3 - ethyl - 2 - *trans* - [β - (2' - pyridyl - 6' - methyl) - vinyl] - chromone.

13. Any one of the compounds according to claim 1 hereinbefore specifically disclosed, except those according to claims 2 to 12.

14. A pharmaceutically acceptable base addition salt of a compound according to any one of claims 2 to 12.



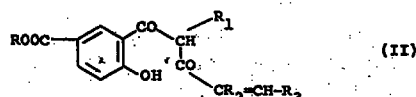
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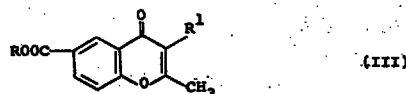
15. A process for the preparation of a compound according to any one of the preceding claims, the processing comprising:

a) cyclising a compound of formula (II)



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wherein R_1 , R_2 , R_3 and R_4 are as defined in claim 1, so obtaining compounds of formula (IA), wherein W is $>C=O$, or
b) reacting a compound of formula (III)



wherein R and R_1 are as defined in claim 1, with an aldehyde of formula (IV)

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wherein R_3 is as defined in claim 1, so obtaining compounds of formula (IA), wherein R_2 is hydrogen, W is $>C=O$, and the vinyl moiety has the *trans*-configuration; and, if desired, converting a resulting compound of formula (IA) wherein W is $>C=O$ into another compound of formula (IA) wherein W is $>C=S$ and/or, if desired, converting a resulting compound of formula (IA) into another compound of formula (IA) by known methods and/or, if desired and applicable, converting a resulting compound of formula (IA) into a pharmaceutically acceptable salt and/or, if desired, converting a salt into a free compound and/or, if desired, separating a mixture of isomers into the single isomers.

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16. A process according to claim 15 substantially as described in any one of the foregoing Examples.

17. A compound or salt according to claim 1 when prepared by a process according to claim 15 or 16.

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18. A pharmaceutical composition comprising a compound or salt according to any one of claims 1 to 14 and 17, and a pharmaceutically acceptable carrier and/or diluent.

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19. A method of treating an allergy in a warm-blooded non-human animal, comprising administering thereto a therapeutically effective dose of a compound or salt according to any one of claims 1 to 14 and 17.

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