

PATENT SPECIFICATION

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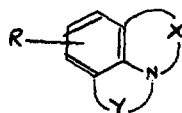


(54) CONTROL OF PLANT DISEASES

(71) We, PFIZER LIMITED, a British Company of Ramsgate Road, Sandwich, Kent, 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 invention relates to the treatment or control of plant diseases and is particularly concerned with the treatment or control of fungal and/or bacterial diseases of the rice plant. It is also concerned with novel compositions for the treatment or control of plant diseases.

According to the invention, a method for the treatment or control of fungal and/or bacterial diseases of plants, especially the rice plant, comprises contacting the plant, or the seeds thereof, with a fungicidally and/or bactericidally effective amount of a pyrrolo-indole, pyrrolo-quinoline or pyridi-quinoline compound of the formula:



I

wherein each of X and Y represents a 2- or 3-carbon chain which completes a saturated or unsaturated pyrrolo- or pyrido- ring;

the carbon chains of X and Y may each be substituted with one or more halogen atoms or lower alkyl or phenyl groups and may include one or more ketone or thioketone groups; and

R represents hydrogen or a lower alkyl, lower alkoxy, lower alkanoyl, benzoyl, hydroxy, lower alkanoyloxy or cyano group or up to

two halogen atoms; or a non-phytotoxic acid addition salt thereof.

In the formula I, when the carbon chains of X and Y are each unsubstituted, they may be any of the groups (a): $-\text{CH}_2\text{CH}_2-$, $-\text{CH}=\text{CH}-$, $-\text{CH}_2\text{CH}_2\text{CH}_2-$ or $-\text{CH}=\text{CHCH}_2-$; and when one or other of them includes one or more ketone or thioketone groups it may be any of the groups (b): $-\text{CH}_2\text{CO}-$, $-\text{CH}_2\text{CH}_2\text{CO}-$, $-\text{CH}=\text{CHCO}-$, $-\text{CO.CO}-$, $-\text{CO.CH}_2\text{CO}-$

(this being tautomeric with $-\text{CO.CH}=\text{C}(\text{OH})-$, $-\text{CO.CO.CO}-$

or the corresponding thio-carbonyl groups. When X or Y are substituted with one or more halogen atoms or lower alkyl or phenyl groups, such halogen or lower alkyl or phenyl replaces hydrogen in the groups (a) or (b).

Some of the compounds of the formula I are known from the chemical literature, the unsubstituted compounds in which R is hydrogen, X is trimethylene and Y is ethylene or trimethylene being known as lilolidine and julolidine, respectively, and oxo-derivatives thereof being known as lilolidones and julolidones, respectively. However, no compound of the formula I has ever been proposed for use in the treatment or control of plant diseases. Moreover, particular classes of compound of the formula I are novel and have been found to be useful in accordance with the present invention. These compounds are claimed *per se* in our copending divisional patent application number 31376/74. (Serial No. 1,394,374).

For the treatment of plant diseases the compounds of the formula (I) may be applied

in the form of a composition comprising the compound together with a diluent or carrier material which is compatible with the intended use of the composition.

5 The compositions may comprise a diluent or carrier, liquid or solid, and be in the form of sprays, including emulsions, slurries, solutions, foams or granules. When applied to rice plants the compositions preferably take
10 the form of sprays of solutions, slurries or emulsions containing compounds of the formula I at a total volume of spray of from about 100 litres to about 600 litres per acre. The concentration of active ingredient in the
15 spray can range from about 5 to about 500 parts per million (ppm). Application at these levels is sufficient to achieve run-off and achieves substantially complete contact of the surface of the rice plant with the active
20 ingredient. The use of a water-insoluble form of the active ingredient is preferred for foliar sprays, rather than a water-soluble form, to avoid their removal from the plants by rain or flooding.

25 For convenience and economy of application the compositions of the invention may consist of the active ingredient formulated into a dust, wettable powder or emulsifiable concentrate.

30 Thus according to a further aspect of the present invention there is provided a composition comprising a compound of the formula (I) together with a diluent or carrier, the composition being in the form of:

- 35 (a) a dust,
(b) a wettable powder, comprising a dust as in (a) above together with a wetting agent and conditioning agent, or
40 (c) an emulsifiable concentrate comprising the compound and an emulsifying agent in a substantially water-immiscible organic solvent.

45 A dust may be made by mixing the proper amount of active ingredient with a diluent or carrier such as talc, clay, calcite, pyrophyllite, diatomaceous earth, walnut shell flour, silica gel, hydrated alumina or calcium silicate to afford a concentration of active ingredient
50 of preferably from 0.25 per cent to 4 per cent by weight. A dust can also be prepared by mixing the diluent or carrier with a solution of the active ingredient in a volatile organic solvent such as benzene or acetone. The solvent
55 is then removed by evaporation and the mixture ground.

Wettable powders, of special value for spray applications, may be made by adding suitable wetting agents and conditioning agents to the dusts.

60 Emulsifiable concentrates may be made by dissolving the active ingredient and an emulsifying agent in a substantially water-immiscible organic solvent. Suitable solvents
65 are toluene, xylene and petroleum oil or an

alkylated naphthalene. The volatile solvents, e.g. toluene, xylene, evaporate after spraying to leave a deposit of the active ingredient upon the plant. The non-volatile solvents leave an oily solution of the active ingredient upon the plant. The emulsifying agent can be cationic, anionic, or non-ionic as is well-known to those skilled in the art. As suitable emulsifiers there may be mentioned ordinary soaps (anionic), lauryl pyridinium chloride (cationic) and polyoxyethylene lauryl ethers (non-ionic), the latter being for example a reaction product of ethylene oxide (ten moles) with dodecyl-alcohol (one mole). Such concentrates may suitably contain from 2 to 50 per cent of the active ingredient and may be mixed with a sufficient volume of water to provide a concentration of active ingredient of from 5 to 500 ppm. For the present purpose, the resulting emulsion may be applied at a rate of from about 100 to 600 litres per acre.

If a water soluble form of the active ingredient is used, it is most conveniently applied in the form of an aqueous spray. Here also, the rate of application is suitable from about 100 to 600 litres per acre of a solution containing 5 to 500 ppm. of active ingredient.

Compositions containing a compound of formula (I) can also be used as seed dressings. When used for the treatment of seeds the prepared forms of the compositions may be dusts, solutions, slurries or emulsions which are applied directly to the seed by appropriate means as by tumbling with the dust or mixing in the solution. For seed protection, levels of active ingredient similar to those previously mentioned, are used e.g. 5 to 500 ppm. of active ingredient in solutions, emulsions, sprays and 0.25 per cent to 4 per cent in dusts

For compositions containing a compound of the formula (I), a wide choice of diluents, emulsifiers, wetting agents or solvents, is available. The compositions may also be applied indirectly by adding them to the water in which the plant is growing, e.g. as controlled time release granules. The particular diluent, emulsifier, solvent or wetting agent best suited for a given formulation may readily be determined by those skilled in the art by simple experiment.

Preferred compositions are those which comprise a compound of formula I in which the carbon chain of either X or Y includes a single ketone or thioketone group, in a position adjacent to the ring nitrogen atom, and R is either hydrogen or halogen, lower alkyl or lower aliphatic acyl substituent in the *para*-position to the ring nitrogen atom. Particularly preferred are those compositions comprising a compound in which X is
—CH₂CO—, —CH₂CH₂CO—,
—CH=CHCO—,

or a corresponding thio-carbonyl group (the —CO— or —CS— group being adjacent to

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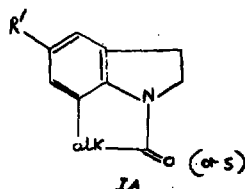
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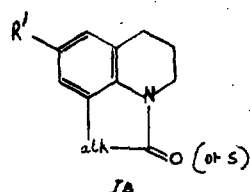
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the ring nitrogen atom), each being optionally substituted with one or more lower alkyl or phenyl groups, and Y is $-\text{CH}_2\text{CH}_2-$ or $-\text{CH}_2\text{CH}_2\text{CH}_2-$, i.e. a compound of the formula:



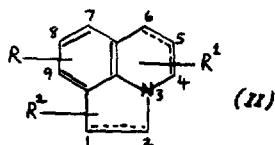
or



where R' is hydrogen, halogen, lower alkyl, lower alkoxy or lower aliphatic acyl and "alk" represents a methylene, ethylene or vinylene group, either of which may be substituted with one or more lower alkyl or phenyl groups.

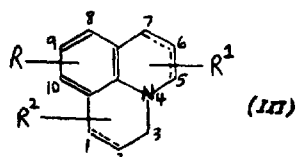
Particularly preferred individual compounds useful in the method and compositions of the present invention include: 2-lilolidone, 4-lilolidone, 1-methyl-2-lilolidone, 8-methyl-2-lilolidone, 8-bromo-4-lilolidone, 8-*tert*-butyl-2-lilolidone, lilolidone-4-thione, 1,2-dihydro-4H-pyrrolo-[3,2,1-*i,j*]-quinolin-4-one, 6-methyl-1,2-dihydro-4H-pyrrolo-[3,2,1-*i,j*]-quinolin-4-one, 3-julolidone, julolidine-3-thione and 1,2-dihydro-3H,5H-pyrido-[3,2,1-*i,j*]-quinolines of the formula:

Novel compounds falling within the scope of formula (I) include pyrrolo-[3,2,1-*i,j*]-quinolines of the formula:



where R is as previously defined other than hydrogen, R^1 and R^2 each represent hydrogen or one or more halogen, lower alkyl, phenyl, oxo or thioxo substituents in the pyrido and pyrrolo rings respectively, and the dotted lines represent an optional bond in each such ring.

Other novel compounds falling within the scope of formula (I) are pyrido-[3,2,1-*i,j*]-quinolines of the formula:



where R is as previously defined other than hydrogen or 9-chloro, R^1 and R^2 each represent hydrogen or substituents (as previously defined) in the respective pyrido rings and the dotted lines represent an optional bond in each such ring.

Compounds of the formulae II and III are claimed *per se* in our copending divisional patent application number 31376/74. (Serial No. 1,394,374).

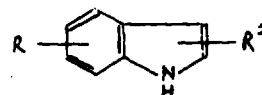
In this specification, "lower" when applied to an alkyl alkoxy, alkanoyl or alkanoyloxy group means that such a group contains up to four carbon atoms. Thus, when R or R' , in formulae I to IB, or R^1 to R^2 in formulae II or III, is or includes a lower alkyl group, that group may, for example, be a methyl, ethyl, propyl, isopropyl, *n*-butyl, *iso*-butyl, *sec*-butyl or *tert*-butyl group, and when R or R' , in formulae I to IB is a lower alkoxy group it may, for example, be a methoxy group or any other alkoxy group containing up to four carbon atoms. When R or R' in formulae I to IB is a lower alkanoyl or alkanoyloxy group it may, for example, be a formyl, acetyl, propionyl, butyryl or isobutyryl group or a corresponding acyloxy group.

Compounds of the formulae I to III which form acid addition salts include those in which there is no oxo or thioxo [=S] group adjacent to the ring nitrogen atom, but are not limited to such compounds. Non-phytotoxic acid addition salts are those which are formed with acids having non-phytotoxic anions, for example, the hydrochloride, hydrobromide, phosphate, nitrate, sulfate, acetate, β,β -dimethylbutyrate, citrate, gluconate, benzoate, propionate, butyrate, sulfo-salicylate, maleate, laurate, malate, fumarate, succinate, oxalate, tartrate, amsonate (4,4'-diamino-stilbene-2'-disulfonate), pamoate (1,1'-methylene-bis-2-hydroxy-3-naphthoate), stearate, 2-hydroxy-3-naphthoate and *p*-toluene-sulfonate salts.

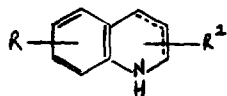
The present invention may be used to treat or control fungal and/or bacterial diseases of plants, particularly (but not limited to) diseases of the rice plant, including the fungal diseases known as rice blast (caused by *Piricularia oryzae*) and leaf blight (caused by *Xanthomonas oryzae*), and the bacterial disease known as sheath blight (caused by *Corticium sasakii*). Other plants, for which the present invention may be used to treat or control fungal or bacterial disease, include tomato and cucumber plants.

The novel compounds included within the scope of the formula I as well as the known compounds may be prepared by a number of methods, including the following:—

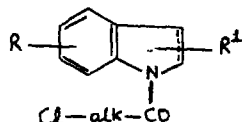
(1) An indole or quinoline compound of the formula:



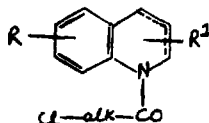
or



- where R and R¹ are as previously defined, with the provisos that R cannot be a substituent in the 7-position of the indole ring or the 8-position of the quinoline ring and cannot be a substituent of such a nature as to de-activate that position or be an acylatable group, and R¹ does not include an oxo or thioxo substituent, may be reacted with a chloro-substituted acid chloride of the formula Cl-alk-COCl, in which "alk" is a methylene, ethylene or vinylene group which may be substituted with one or more lower alkyl or phenyl groups, in the presence of a base, e.g. trimethylamine, to form a compound of the formula:



or



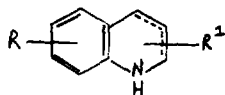
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which is then cyclised in the presence of aluminium chloride to form a compound of the formula II or III, in which R¹ does not include an oxo or thioxo substituent, but R² includes an oxo substituent adjacent to the ring nitrogen atom and may also include one or more lower alkyl or phenyl substituents. If in this method R includes any alkoxy group, such group is converted under the conditions of cyclisation to a hydroxyl group.

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(2) A quinoline compound of the formula:

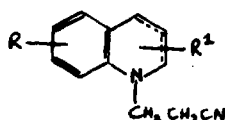


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where R and R¹ are as defined for method (1), may be reacted with acrylonitrile or a β -halo-propionitrile of the formula



(in which X is halogen) to form a compound of the formula:



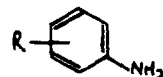
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which is hydrolysed to convert the nitrile group to a carboxy group and then cyclised

in the presence of a dehydrating agent, e.g. phosphoric anhydride, to form a compound of formula III in which R² is 1-oxo and R¹ does not include an oxo or thioxo substituent.

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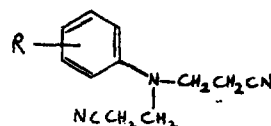
(3) An aniline derivative of the formula:



where R is as previously defined, with the provisos that it cannot be a substituent in the 2- or 6-position of the benzene ring and cannot be a substituent of such a nature as to de-activate either of these positions or be an acylatable group, may be reacted with 2 moles of acrylonitrile or a β -halo-propionitrile as defined in method (2) to form a compound of the formula:

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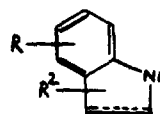
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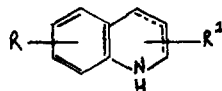
which is then hydrolysed and cyclised as in method (2) to form a compound of formula III in which R¹ is 6-oxo and R² is 1-oxo.

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(4) A compound of the formula:



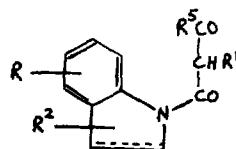
or



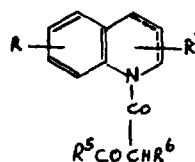
where R and R¹ are as defined for methods (1) or (2) and R² is as previously defined with the proviso that it does not include an oxo or thioxo substituent, may be reacted with an aceto-acetic acid ester of the formula R⁵COCHR⁶COOC₂H₅, in which R⁵ is a lower alkyl or phenyl group and R⁶ is hydrogen or a lower alkyl group, to form a compound of the formula:

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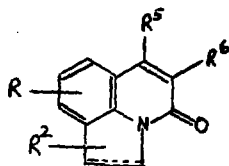
or



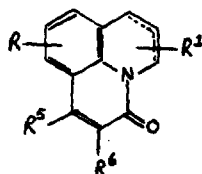
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which is then cyclised in the presence of a dehydrating agent, e.g. concentrated sulphuric acid or polyphosphoric acid, to form a compound of the formula:

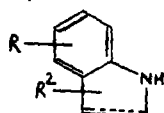
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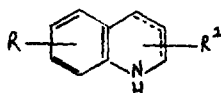
or



(5) A compound of the formula:

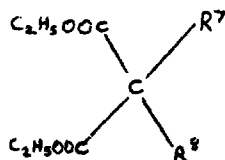


10 or



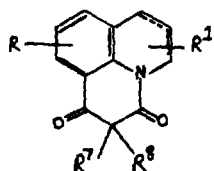
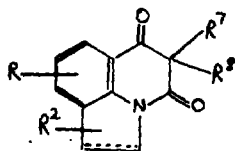
where R, R¹ and R² are as defined for methods (1), (2) or (3), is reacted with a malonic acid ester of the formula:

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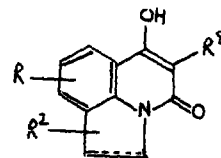


in which R⁷ and R⁸ are each hydrogen or a lower alkyl or phenyl group, to form a compound of the formula:

20 or

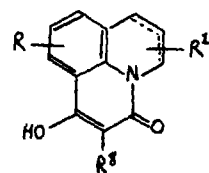


which, in the case where R⁷ is hydrogen, are tautomeric with the formulae:



and

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respectively.

(6) A compound of the formula II or III, in which R¹ and/or R² includes one or more oxo substituents, may be reduced with lithium aluminium hydride to replace the oxo substituent(s) with hydrogen.

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(7) A compound of the formula II or III, in which R¹ and/or R² includes one or more oxo substituents, may be treated with diphosphorus pentasulphide to replace the oxo substituent(s) with sulphur.

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(8) A compound of formula I, in which X or Y includes an unsaturated group, may be converted to the corresponding saturated compounds by catalytic hydrogenation, which may also result in replacement of halogen substituents in X or Y by hydrogen.

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(9) A compound of the formula I, in which R is hydrogen, may be converted to a compound of the same formula, but in which R is halogen, alkyl, alkanoyl or benzoyl, by well-known techniques of nuclear aromatic halogenation, alkylation or acylation, respectively, and R may then be converted to other groups by well-known reaction sequences, including (for example) replacement of halogen by cyano.

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Aromatic halogenation, e.g. chlorination with gaseous chlorine or with dichloro-urethane, may also result in the introduction of halogen into R¹ and R², especially at positions adjacent to any oxo group(s). Such halogen may subsequently be removed, if not required, by selective reduction to replace it by hydrogen, converted to other groups, e.g. to an oxo group by hydrolysis of a gem-dihalo group, or replaced by phenyl by Friedel-Crafts reaction with benzene.

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(1) A compound of the formula I, in which R includes one or more hydroxyl groups, may be converted to lower aliphatic acyl esters thereof by conventional esterification techniques.

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(11) Compounds of the formula II or III, in which R¹ or R² includes one or more halogen substituents, may also be formed from

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the corresponding hydroxy compounds by conventional methods for the conversion of alcohols to halides, e.g. treatment with phosphorus or thionyl halides. The hydroxy compound starting material may, for example, be the enolic forms of β -diketones, i.e. compounds in which R^1 or R^2 includes two oxo substituents separated by a methylene group, which may be substituted by an alkyl or phenyl group.

(12) Non-phytotoxic acid addition salts of any compound of the formula I, which is sufficiently basic to form such salts, may be formed by conventional methods, e.g. by dissolving the compound in a suitable solvent and adding the appropriate acid, either in a solvent also, or as the acid itself if liquid or gaseous, to precipitate the required salt.

The preparation of the compounds of the Formula I is illustrated by the following Examples, in which temperatures are given in $^{\circ}\text{C}$.

EXAMPLE 1.

(A) To a stirred solution of 6-methyl-1,2,3,4-tetrahydroquinoline (7.4 g) in dry benzene (120 ml) containing triethylamine (8.4 ml) was added over a period of $\frac{1}{2}$ hour chloroacetyl chloride (6.0 g, 4.3 ml). Stirring was continued for a further 2 hours, after which the precipitate of triethylamine hydrochloride was filtered off and the benzene filtrate was washed in turn with 2N hydrochloric acid (100 ml) and water (2×100 ml). The benzene solution was then dried over anhydrous magnesium sulphate and evaporated *in vacuo* to afford a gum (9.5 g), most of which was used directly in the next stage (B).

A portion (3.5 g) of the aforementioned gum was purified by passage through a silica column using chloroform as the eluent, and the chloroform solution was evaporated *in vacuo* to an oil which eventually solidified. A sample was recrystallised from petroleum ether (b.p. $40-60^{\circ}$) to yield a solid, m.p. $58-60^{\circ}$, shown by standard analytical techniques to be 1-chloroacetyl-6-methyl-1,2,3,4-tetrahydroquinoline.

Analysis:—

Found:

C, 64.09; H, 6.26; N, 6.22%.

Calculated for $\text{C}_{12}\text{H}_{14}\text{NOCl}$:

C, 64.46; H, 6.27; N, 6.27%.

(B) The gummy product of the previous stage (6.0 g) and finely powdered anhydrous aluminium chloride (5.0 g) were mixed at room temperature, whereupon the temperature of the mixture rose to about 130° . The mixture was then warmed in an oil bath at 140° for 30 minutes (during which time the temperature within the mixture rose to 170°) and thereafter poured while still hot onto a mixture of ice and hydrochloric acid. Extraction of the aqueous solution with chloroform (2×50 ml) was followed by washing the organic solution with water and drying over anhydrous magnesium sulphate. Evaporation of the chloroform layer *in vacuo* afforded an oil (3.7 g) which solidified. The crude solid product was recrystallised from petroleum ether (b.p. $60-80^{\circ}$) to yield 1.6 g of 8-methyl-1,2,5,6-tetrahydro-4H-pyrrolo-[3,2,1-*i,j*]-quinolin-2-one, m.p. $115-7^{\circ}$.

Analysis:—

Found:

C, 77.01; H, 6.93; N, 7.47%.

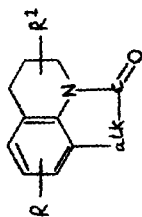
Calculated for $\text{C}_{12}\text{H}_{13}\text{NO}$:

C, 77.01; H, 6.95; N, 7.49%.

EXAMPLES 2 to 4.

By procedures similar to that described in Example 1, the following novel compounds were prepared starting from the appropriate substituted 1,2,3,4-tetrahydroquinoline and chloroacetyl chloride.

Similarly the known compounds 1,2,5,6-tetrahydro-4H-pyrrolo-[3,2,1-*i,j*]-quinolin-2-one (2-lilolidone), and its 1-phenyl and 1-methyl derivatives, were prepared from 1,2,3,4-tetrahydroquinoline and chloroacetyl chloride, α -chloro-phenylacetyl chloride and α -chloropropionyl chloride, respectively; and the known compound 1,2,5,6-tetrahydro-4H-pyrrolo-[3,2,1-*i,j*]-quinolin-4-one (4-lilolidone) was prepared from indoline and β -chloropropionyl chloride.



Example	R	R'	alk	m.p. °C	Analysis (theoretical in brackets) C % H % N %
2	9-CH ₃	H	-CH ₂ -CH ₂ -	63-5°	77.32 (77.58) 7.46 7.57 6.62 6.96
3	8-CH ₃	1-H	-CH- Ph	80-81°	82.22 (82.20) 6.52 6.47 5.66 5.33
4	H	4-CH ₃	-CH ₂ -	65-7°	76.96 (77.01) 7.04 6.95 7.27 7.49

EXAMPLE 5.

Chlorine was passed into a solution of 1,2,5,6 - tetrahydro - 4H - pyrrolo-[3,2,1-i,j] - quinolin - 2 - one (5.0 g) in chloroform (50 ml) for a period of 20 minutes, and the resultant pale orange solution was then concentrated by evaporation *in vacuo* to an oil. A small sample was crystallised by trituration in petroleum ether, and the crystals were used as seeds to bring about total crystallisation of the oil. The crystalline solid was recrystallised from a mixture of benzene and petroleum ether, yielding 1,1,8-trichloro - 1,2,5,6 - tetrahydro - 4H - pyrrolo-[3,2,1-i,j] - quinolin - 2 - one, m.p. 148-9°.

Analysis:—

Found:
C, 47.30; H, 2.76 N, 5.03%
Calculated for C₁₁H₈Cl₃NO:
C, 47.70; H, 2.90; N, 5.07%

EXAMPLE 6.

1,2,5,6 - Tetrahydro - 4H - pyrrolo-[3,2,1-i,j] - quinolin - 2 - one (5 g) was dissolved in 80% acetic acid and dichloro-urethane (4.5 g, 5.5 ml) was added whereupon the temperature of the solution was observed to rise to about 60°. The solution was stirred for 4 hours after which water (10 ml) was added, resulting after a few minutes in the precipitation of a white powder. The latter

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was collected by filtration and recrystallised in turn from glacial acetic acid and a mixture of benzene and petroleum ether, yielding what was believed from infra-red and nuclear magnetic resonance spectroscopic evidence to be 1,1,7,8 - tetrachloro - 1,2,5,6 - tetrahydro-4H - pyrrolo - [3,2,1-i,j] - quinolin - 2 - one, m.p. 167—170°.

Analysis:—

Found:

C, 43.29; H, 2.61; N, 4.66%

Calculated for $C_{11}H_7Cl_4NO$:

C, 42.50; H, 2.27; N, 4.51%

EXAMPLE 7.

To a solution of 1,2,5,6 - tetrahydro - 4H - pyrrolo - [3,2,1-i,j] - quinolin - 4 - one (1.0 g) in carbon tetrachloride (20 ml) was added a solution of bromine (0.35 ml) in the same solvent (5 ml). After a few minutes a solid separated, and this was filtered off and recrystallised from a mixture of water and methanol to afford 0.75 g of 8-bromo-1,2,5,6-tetrahydro - 4H - pyrrolo - [3,2,1-i,j] - quinolin-4-one, m.p. 107—9°.

Analysis:—

Found:

C, 52.36; H, 4.00; N, 5.66%

Calculated for $C_{11}H_9BrNO$:

C, 52.40; H, 4.00; N, 5.56%

EXAMPLE 8.

A solution of 1,2,5,6 - tetrahydro - 4H - pyrrolo - [3,2,1-i,j] - quinolin - 2 - one (5.0 g) and bromine (1.5 ml) in chloroform (15 ml) was warmed to 45° and maintained at that temperature. Within 5 minutes a precipitate had formed and this was collected by filtration and recrystallised from 75% aqueous acetic acid solution, yielding 8-bromo 1,2,5,6-tetrahydro - 4H - pyrrolo - [3,2,1-i,j] - quinolin-2-one, m.p. 125—6°.

Analysis:—

Found:

C, 53.09; H, 4.02; N, 5.59%

Calculated for $C_{11}H_9BrNO$:

C, 52.30; H, 3.99; N, 5.56%

EXAMPLE 9.

A solution of bromine in chloroform (1 ml taken from 5.52 ml in 10 ml) was slowly added to a solution of 1 - phenyl - 1,2,5,6 - tetrahydro - 4H - pyrrolo - [3,2,1-i,j] - quinolin-2-one (2.49 g) in chloroform (50 ml) whereupon an exothermic reaction ensued with evolution of hydrogen bromide. The mixture was warmed for $\frac{1}{2}$ hour on a steam bath after which the solution was evaporated to dryness *in vacuo* and a portion of the solid was submitted to nuclear magnetic resonance spectroscopy. The evidence suggested incomplete reaction, and so more bromine in chloroform solution was added to a solution of the residue in chloroform with warming and the re-

action allowed to continue for a further short period of time.

The solution was evaporated *in vacuo* and the solid residue recrystallised from a mixture of cyclohexane and petroleum ether, affording 1,8 - dibromo - 1 - phenyl - 1,2,5,6-tetrahydro - 4H - pyrrolo - [3,2,1-i,j] - quinolin-2-one, m.p. 119.5—120.5°.

Analysis:—

Found:

C, 51.04; H, 3.50; N, 3.41%

Calculated for $C_{17}H_{13}NOBr_2$:

C, 50.15; H, 3.22; N, 3.44%

EXAMPLE 10.

By a procedure similar to that described in Example 9, 1,8 - dibromo - 1 - methyl-1,2,5,6 - tetrahydro - 4H - pyrrolo - [3,2,1-i,j] - quinolin - 2 - one, m.p. 138—9°, was prepared by bromination of 1 - methyl-1,2,5,6 - tetrahydro - 4H - pyrrolo - [3,2,1-i,j] - quinolin-2-one.

Analysis:—

Found:

C, 42.14; H, 3.58; N, 4.00%

Calculated for $C_{12}H_{11}NOBr_2$:

C, 41.77; H, 3.21; N, 4.06%

EXAMPLE 11.

To a solution of 1,2,5,6 - tetrahydro - 4H - pyrrolo - [3,2,1-i,j] - quinolin - 2 - one (10 g) in chloroform (30 ml) was added bromine (3.1 ml), after which the solution was allowed to stand at room temperature. Within a few minutes a precipitate had formed, and this was filtered off, washed with chloroform and dried, the yield of 8-bromo-compound being 10 g.

The 8 - bromo - 1,2,5,6 - tetrahydro - 4H - pyrrolo - [3,2,1-i,j] - quinolin - 2 - one (10 g) was suspended in chloroform and chlorine was bubbled into the suspension, whereupon dissolution rapidly occurred. Chlorine passage was continued for about 20 minutes after which the solution was evaporated *in vacuo* and the resulting gummy solid was triturated in petroleum ether. Recrystallisation of the resultant solid afforded 8 - bromo - 1,1 - dichloro - 1,2,5,6 - tetrahydro - 4H - pyrrolo - [3,2,1-i,j] - quinolin - 2 - one, buff coloured crystals, m.p. 149—150°.

Analysis:—

Found:

C, 40.96; H, 2.57; N, 4.32%

Calculated for $C_{11}C_2BrCl_2NO$:

C, 41.10; H, 2.51; N, 4.36%

EXAMPLE 12.

A mixture of 1,2,5,6 - tetrahydro - 4H - pyrrolo - [3,2,1-i,j] - quinolin - 4 - one (1.0 g), propionic acid (1.0 ml) and polyphosphoric acid (phosphorus pentoxide content 82—5%, 80 g) was heated on a steam bath for 3 hours and then poured while still hot into water. The mixture was then stirred until

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EXAMPLES 13 to 19.

By procedures similar to that described in Example 12, the compounds of Examples 13 to 18 were prepared by acylations with appropriate carboxylic acids of appropriately substituted or unsubstituted 1,2,5,6-tetrahydro-4H-pyrrolo-[3,2,1-ij]-quinolines in the presence of polyphosphoric acid. The compound of Example 19 was prepared by the benzoylation of 1,2,5,6-tetrahydro-4H-pyrrolo-[3,2,1-ij]-quinolin-2-one under similar dehydrating conditions.

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appearing homogeneous and extracted with diethyl ether (2 X 100 ml), the ethereal layer then being separated, washed with water, dried over anhydrous magnesium sulphate and evaporated *in vacuo* to dryness. Crystallisation of the resultant solid from ethanol afforded 0.45 g of 8-propionyl-1,2,5,6-tetrahydro-4H-pyrrolo-[3,2,1-ij]-quinolin-4-one, m.p. 144—7°.

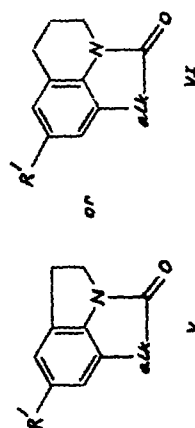
Analysis:—

Found:

C, 73.34; H, 6.59; N, 6.11%

Calculated for $C_{14}H_{11}NO_2$:

C, 73.67; H, 6.47; N, 5.89%



Example	Formula	alk	R'	m.p. °C	Analysis (theoretical in brackets) C % H % N %		
13	VI	-CH- CH ₃	C ₂ H ₅ CO-	115-6°	73.00 (72.73)	7.06 7.12 (based on C ₁₅ H ₁₁ NO ₂ ·½H ₂ O)	5.56 5.65
14	VI	-CH- CH ₃	CH ₃ (CH ₂) ₂ CO-	102-4°	74.52 (74.68)	7.40 7.44	5.69 5.44
15	VI	-CH ₂ -	CH ₃ CO-	154-6°	72.33 (72.50)	6.14 6.05	6.46 6.52

TABLE (Continued)

Example	Formula	alk	R'	m.p. °C	Analysis (theoretical in brackets)	
					C %	H % N %
16	VI	-CH ₂ -	C ₂ H ₅ CO-	169-170°	73.99 (73.34)	6.26 6.59 5.86 6.11
17	V	-CH ₂ -CH ₂ -	CH ₃ CO-	97-100°	71.77 (72.50)	6.07 6.05 5.87 6.52
18	VI	-CH- CH ₃	CH ₃ CO-	113-5°	73.46 (73.34)	6.68 6.59 6.10 6.11
19	VI	-CH ₂ -	C ₆ H ₅ CO-	127-130°	77.17 (76.96)	5.31 5.70 5.24 5.28

EXAMPLE 20.

To a suspension of 1,1,8-trichloro-1,2,5,6-tetrahydro - 4H - pyrrolo - [3,2,1-*ij*] - quinolin-2-one (prepared as in Example 5) (2.0 g) in 50% aqueous methanol (100 ml) contained in a bomb was added anhydrous sodium acetate (0.5 g). The suspension was heated for 24 hours at 100°. The resulting dark red solution containing a little undissolved material was freed of the latter by filtration and concentrated by evaporation *in vacuo*. A solid precipitate was collected by filtration and recrystallised from a mixture of benzene and petroleum ether, affording deep red crystals of 8 - chloro - 1,2,5,6 - tetrahydro-4H - pyrrolo - [3,2,1-*ij*] - quinolin - 1,2-dione, m.p. 185°.

Analysis:—

Found:

C, 59.7; H, 3.66; N, 6.17%
Calculated for C₁₁H₈ClN₂O:
C, 59.45; H, 3.64; N, 6.32%

20

EXAMPLE 21.

By a procedure similar to that described in the previous Example, 8 - bromo - 1,1 - dichloro - 1,2,5,6 - tetrahydro - 4H - pyrrolo - [3,2,1-*ij*] - quinolin - 2 - one (prepared as in Example 11) was hydrolysed and yielded 8 - bromo - 1,2,5,6 - tetrahydro - 4H - pyrrolo - [3,2,1-*ij*] - quinolin - 1,2 - dione, as dark red crystals, m.p. 185-7°.

25

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Analysis:—

Found:

C, 49.90; H, 3.10; N, 5.42%

Calculated for $C_{11}H_8BrNO_2$:

5 C, 49.60; H, 3.30; N, 5.27%

EXAMPLE 22.

To a stirred suspension of 1,1,8-trichloro-1,2,5,6 - tetrahydro - 4H - pyrrolo-[3,2,1-i,j] - quinolin - 2 - one (prepared as in Example 5) (5 g) in acetic acid (100 ml) was added zinc dust (5 g) at such a rate as to keep the temperature of the mixture below 50°. After complete addition of zinc, the mixture was refluxed with stirring for 5 hours. The supernatant liquid was decanted into water whereupon a solid precipitated. The precipitate was collected by filtration, recrystallised from cyclohexane and dried *in vacuo*, yielding 2 g of 8 - chloro - 1,2,5,6-tetrahydro - 4H - pyrrolo - [3,2,1-i,j]-quinolin-2-one, m.p. 120—2°.

Analysis:—

Found:

C, 63.60; H, 5.13; N, 6.74%

25 Calculated for $C_{11}H_8ClNO$:

C, 63.70; H, 4.88; N, 6.75%

EXAMPLE 23.

To a solution of 1,1,8 - trichloro - 1,2,5,6-tetrahydro - 4H - [3,2,1-i,j] - quinolin - 2-one (prepared as in Example 5) (4.5 g) in dry benzene (100 ml) was added aluminium chloride (4.3 g), and the mixture was then heated, gently at first, to reflux whereafter refluxing was continued for 2 hours. Throughout this period hydrogen chloride was evolved.

The mixture was then allowed to cool to room temperature, poured into water and the resultant solid filtered, washed with diethyl ether and crystallised from benzene, affording crystals, m.p. 265—7°. A second crop of crystals was produced on addition of petroleum ether to the benzene filtrate, and this was collected by filtration. Both crops were seen to be pure from thin layer chromatography evidence and so were combined, and constituted the total yield of 8-chloro-1,1-diphenyl-1,2,5,6 - tetrahydro - 4H - pyrrolo-[3,2,1-i,j]-quinolin-2-one.

50 Analysis:—

Found:

C, 76.53; H, 5.39; N, 3.45%

Calculated for $C_{23}H_{18}ClNO$:

C, 76.80; H, 5.04; N, 3.89%

EXAMPLE 24.

55 A mixture of 1,2,5,6 - tetrahydro - 4H-pyrrolo - [3,2,1-i,j] - quinolin - 2 - one (1.73 g), *tert*-butyl chloride (5 ml) and aluminium chloride (~0.5 g) was heated at about 60° for 2 hours, at the end of which period the whole had virtually solidified. It was then added to water and the suspension was ex-

tracted with chloroform, the chloroform solution then being separated, dried over anhydrous magnesium sulphate and evaporated *in vacuo* to dryness. The solid was recrystallised from 60—80° petroleum ether and submitted to gas liquid chromatography, the evidence suggesting that there was present a mixture of 1,2,5,6 - tetrahydro - 4H - pyrrolo-[3,2,1-i,j]-quinolin-2-one and its 8-*tert*-butyl derivative.

Dissolution of the solid in hot petroleum mixture and subsequent cooling resulted in precipitation of a solid, believed to be an impurity. The precipitate was removed by filtration and the filtrate evaporated *in vacuo* to dryness, the resultant solid then being submitted to gas liquid chromatography, the evidence from which suggesting a ~96% pure product. Standard analytical techniques confirmed that this product was 8-*tert*-butyl-1,2,5,6 - tetrahydro - 4H - pyrrolo-[3,2,1-i,j]-quinolin-2-one, m.p. 122—4°.

Analysis:—

Found:

C, 80.09; H, 8.10; N, 5.86%

Calculated for $C_{17}H_{18}NO$:

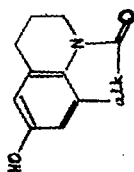
C, 78.90; H, 8.30; N, 6.12%

EXAMPLE 25.

(A) To a stirred solution of 6-methoxy-1,2,3,4-tetrahydroquinoline (4.02 g) and triethylamine (3.0 g) in dry benzene (80 ml) was added dropwise over 30 minutes chloroacetyl chloride (2.82 g). Stirring was continued for a further 3 hours at room temperature, after which the triethylamine hydrochloride in suspension was removed by filtration and the benzene solution filtrate was washed in turn with 2N hydrochloric acid and water, and then dried over anhydrous magnesium sulphate. Evaporation of the benzene solution *in vacuo* afforded an oil (4.0 g) which could not be crystallised, and so it was used directly as such in the next stage. The product in crude form was 1 - chloroacetyl - 6 - methoxy - 1,2,3,4-tetrahydroquinoline. The procedure was repeated to obtain a further quantity of the crude product.

(B) The product of (A) (9.0 g) was mixed with powdered anhydrous aluminium chloride (18.0 g) and the mixture was gradually heated to 100°, fumes of hydrogen chloride being evolved, and heating was continued until an oil-bath temperature of 200° had been attained, at which point the mixture was a molten mass. The reaction mixture was heated for a further 1 hour at an oil bath temperature of 200°, and then cooled to room temperature, the mixture by then having solidified. The ground mixture

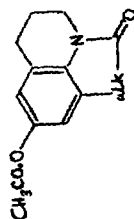
- 5 was added to an ice-water mixture, and the aqueous solution then extracted with chloroform, the chloroform solution then being extracted with sodium hydroxide solution. On standing, the latter afforded a precipitate, and the suspension was extracted with fresh chloroform. The chloroform solution was dried over anhydrous magnesium sulphate and evaporated to dryness *in vacuo*, the resultant solid (3.5 g) then being recrystallised from absolute ethanol to afford 8 - hydroxy - 1,2,5,6 - tetra-
- 10
- 15 hydro - 4H - pyrido - [3,2,1-i,j] - quinolin-2-one, m.p. 200—202°.
Analysis:—
Found: C, 69.09; H, 5.96; N, 7.44%
Calculated for C₁₁H₇NO₂:
C, 69.82; H, 5.86; N, 7.40%
EXAMPLES 26 and 27.
- 20 By procedures similar to that described in Example 25, the following compounds were prepared starting from 6-methoxy-1,2,3,4-tetrahydroquinoline and the appropriate chloroacyl chloride.
- 25



Example	alk	m.p. °C	Analysis (theoretical in brackets)		
			C %	H %	N %
26	$\begin{array}{c} \text{--CH--} \\ \\ \text{CH}_3 \end{array}$	197–200°	70.23 (70.91)	6.50 6.45	6.82 6.89)
27	$\text{--CH}_2\text{CH}_2\text{--}$	230–5°	70.52 (70.91)	6.56 6.45	6.53 6.89)

- EXAMPLE 28.
- 30 9 - Hydroxy - 2,3,6,7 - tetrahydro - 1H,5H-pyrido - [3,2,1-i,j] - quinolin - 3 - one (the compound of Example 27) (0.5 g) was added to benzene (20 ml) containing sodium acetate (0.1 g) and acetic anhydride (0.3 ml), and the mixture was refluxed for 3 hours. After cooling, the sodium acetate was removed by filtration and the solution was evaporated *in vacuo* to dryness. The resultant solid was washed with 60—80° petroleum ether and crystallised from a mixture of benzene and 60—80° petroleum ether to yield 0.33 g of 9 - acetox - 2,3,6,7 - tetrahydro - 1H,5H-
- 35
- 40

- pyrido - [3,2,1-*i,j*] - quinolin - 3 - one as
pale yellow crystals, m.p. 124—6°.
- Analysis:—
- Found: C, 68.56; H, 6.17; N, 5.68%
Calculated for $C_{14}H_9NO$:
C, 68.10; H, 6.24; N, 5.28%
- 5
- EXAMPLES 29 and 30.
By procedures similar to that described in
Example 28, the following two compounds
were prepared starting from the compounds
of Examples 25 and 26, respectively.
- 10



Example	alk	m.p. °C	Analysis (theoretical in brackets)	
			C %	H %
29	—CH ₂ —	140—2°	67.71 (67.52)	5.71 5.67
				6.33 6.06)
30	—CH— CH ₃	130—1°	68.55 (68.10)	6.16 6.24
				5.71 5.28)

- EXAMPLE 31.
- 15 A solution of 8-bromo-1,2,5,6-tetrahydro-4H - pyrrolo - [3,2,1-*i,j*] - quinolin - 4-one (prepared as in Example 7) (1.5 g) and cuprous cyanide (0.63 g) in N-methyl-2-pyrrolidone (13 ml) was refluxed for 6 hours, and then allowed to cool to room temperature, whereupon a precipitate had formed. The precipitate (700 mg) was collected by filtra-
- tion and 400 mg thereof recrystallised from ethanol, yielding 250 mg of 8-cyano-1,2,5,6-tetrahydro - 4H - pyrrolo - [3,2,1-*i,j*] - quinolin-4-one, m.p. 204—5°.
- Analysis:—
- Found: C, 72.96; H, 5.02; N, 14.20%
Calculated for $C_{12}H_9N_2O$:
C, 72.71; H, 5.09; N, 14.13%
- 20
- 25
- 30

EXAMPLE 32.

(A) A solution of 6 - methyl - 1,2,3,4-tetrahydroquinoline (3.0 g) and ethyl acetoacetate (2.8 g) in xylene (7.0 ml) containing 2 drops of dry pyridine was refluxed for 12 hours. The solution was then allowed to cool to room temperature, washed in turn with 2N hydrochloric acid (2 × 20 ml) and water (2 × 20 ml), dried over anhydrous magnesium sulphate and evaporated under reduced pressure at 100° to dryness, yielding 1 - acetoacetyl - 6-methyl - 1,2,3,4 - tetrahydroquinoline (1.7 g) as a crude solid, to be used directly in the next stage.

(B) The product of (A) (1.6 g) was slowly added to concentrated sulphuric acid (2 ml) with stirring, keeping the temperature below 100°. The mixture was then heated on a steam bath for 15 minutes and poured onto ice, the aqueous solution then being basified by addition of dilute sodium hydroxide solution and extracted with chloroform. Evaporation of the previously dried chloroform solution *in vacuo* yielded a solid, which was crystallised from a mixture of benzene and 60—80° petroleum ether to afford crystals (0.7 g) of 1,9 - dimethyl - 6,7-dihydro - 5H - pyrido - [3,2,1-*i,j*] - quinolin-3-one, m.p. 136—7°.

Analysis:—

Found:

C, 79.34; H, 6.90; N, 6.61%

Calculated for $C_{14}H_{13}NO$:

C, 78.84; H, 7.09; N, 6.57%

EXAMPLE 33.

By a procedure similar to that described in Example 32, 1 - methyl - 9 - methoxy-6,7 - dihydro - 5H - pyrido - [3,2,1-*i,j*] - quinolin-3-one, m.p. 115—7°, was prepared starting from 6 - methoxy - 1,2,3,4 - tetrahydroquinoline and ethyl acetoacetate.

Analysis:—

Found:

C, 73.34; H, 6.60; N, 6.03%

Calculated for $C_{14}H_{13}NO_2$:

C, 72.76; H, 6.59; N, 6.11%

EXAMPLE 34.

(A) A mixture of indoline (9.5 g) and ethyl α -ethylacetoacetate was refluxed for 1 hour and then submitted to a distillation to remove ethanol formed in the reaction, 2 ml thereof being collected. The residual oil was then poured into water and the mixture acidified by addition of dilute hydrochloric acid and extracted with chloroform, the organic solution then being dried over anhydrous magnesium sulphate and evaporated *in vacuo* to afford an oil (22.5 g) which

solidified on standing. The crude product, 1 - (α - ethylacetoacetyl)-indoline was then crystallised from cyclohexane prior to use in the next stage.

(B) The product of (A) (2.0 g) and polyphosphoric acid (2.0 g) were heated together at 150° for 1 hour and then poured into water. The mixture was extracted with chloroform, the organic solution then being washed with water, dried over anhydrous magnesium sulphate and evaporated *in vacuo* to afford an oil, which subsequently solidified on standing. Crystallisation of the crude product from cyclohexane yielded 5-ethyl - 6 - methyl - 1,2 - dihydro - 4H-pyrrolo - [3,2,1-*i,j*] - quinolin - 4-one, m.p. 83—4°.

Analysis:—

Found:

C, 78.78; H, 7.13; N, 6.10%

Calculated for $C_{14}H_{13}NO$:

C, 78.84; H, 7.09; N, 6.57%

EXAMPLE 35.

By a procedure similar to that described in Example 34, 6 - phenyl - 1,2 - dihydro - 4H-pyrrolo - [3,2,1-*i,j*] - quinolin - 4 - one, m.p. 177.5—178.5°, was prepared starting from indoline and ethyl benzoylacetate.

Analysis:—

Found:

C, 82.43; H, 5.29; N, 5.65%

Calculated for $C_{17}H_{13}NO$:

C, 82.56; H, 5.30; N, 5.66%

EXAMPLE 36.

A mixture of indoline (5.95 g) and α -methyl diethyl malonate (8.7 g) was refluxed under an air condenser for 2 hours, after which time all the ethanol formed in the reaction had evolved and excess α -methyl diethyl malonate was distilling off. The mixture was allowed to cool to room temperature, the whole mass solidifying by this stage, and the solid was crystallised from acetic acid to yield 6.3 g of 6 - hydroxy - 5 - methyl - 1,2-dihydro - 4H - pyrrolo - [3,2,1-*i,j*] - quinolin-4-one, m.p. 300°, with decomposition.

Analysis:—

Found:

C, 71.25; H, 5.56; N 6.62%

Calculated for $C_{17}H_{13}NO_2$:

C, 71.62; H, 5.57; N, 6.96%

This compound is the enolic form of 5-methyl-1,2,5,6 - tetrahydro - 4H - pyrrolo - [3,2,1-*i,j*] - quinolin-4,6-dione.

EXAMPLE 37.

By a procedure similar to that described in Example 36, 1 - hydroxy - 2 - methyl - 6,7-

dihydro - 5H - pyrido - [3,2,1-i,j] - quinolin-3-one, m.p. 200—2°, was prepared from tetrahydroquinoline and α -methyl diethyl malonate.

5 *Analysis*:—

Found:

C, 72.59; H, 5.96; N, 6.62%

Calculated for $C_{13}H_{13}NO_2$:

C, 72.54; H, 6.04; N, 6.51%

10 This compound is the enolic form of 2-methyl - 2,3,6,7 - tetrahydro - 1H,5H-pyrido-[2,3,1-i,j]-quinolin-1,3-dione.

EXAMPLE 38.

15 1 - Hydroxy - 2 - methyl - 6,7 - dihydro-5H - pyrido - [3,2,1-i,j] - quinolin - 3 - one (prepared as in Example 37) (2.8 g) and phosphorus pentachloride (2.5 g) were intimately mixed by grinding together with a pestle and mortar. To the powder was added
20 a small amount of phosphoryl chloride, and the mixture was then gently heated to 120° and maintained at that temperature for $\frac{1}{2}$ hour, after which the resultant melt was allowed to cool to room temperature and dis-
25 solved in concentrated hydrochloric acid. The solution was diluted by addition to water (50 ml) and basified with sodium hydroxide solution, whereupon a brown precipitate formed. Collection of the precipitate by filtra-
30 tion and two recrystallisations from cyclohexane yielded 300 mg of 1-chloro-2-methyl-6,7 - dihydro - 5H - pyrido - [3,2,1-i,j]-quinolin-3-one, m.p. 138—140°.

Analysis:—

35 Found:

C, 66.90; H, 5.24; N, 6.21%

Calculated for $C_{13}H_{12}ClNO$:

C, 66.45; H, 5.11; N, 5.96%

EXAMPLE 39.

Phosphorus pentasulphide (1.1 g) was added
40 in small portions over a 15 minute period to a solution of 1,2,5,6 - tetrahydro - 4H-pyrrolo - [3,2,1-i,j] - quinolin - 4 - one (1.73 g) in dry pyridine (12.5 ml) with shaking.
45 The solution was then refluxed for 10 minutes, cooled, and poured into water, the resultant precipitate then being collected by filtration and dried. Produced was 1.3 g of crude product, m.p. 115—7°.

Soxhlet extraction with 60—80° petroleum
50 ether afforded, after evaporation of the solution to dryness, 1.0 g of pale yellow crystals. Recrystallisation of the latter from *n*-hexane afforded 0.6 g of 1,2,5,6 - tetrahydro - 4H-pyrrolo - [3,2,1-i,j] - quinolin - 4 - thione,
55 m.p. 126—126.5°.

Analysis:—

Found:

C, 69.60; H, 5.89; N, 7.30%

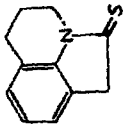
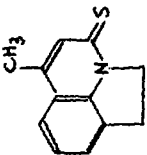
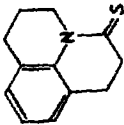
Calculated for $C_{11}H_{11}NS$:

C, 69.80; H, 5.86; N, 7.41%

EXAMPLES 40 to 42.

By procedures similar to that described in
65 Example 39, the following thiones were prepared starting from the corresponding oxo compounds and phosphorus pentasulphide. The oxo compound starting materials were the known compounds 2-lilolidone, 6 - methyl-1,2 - dihydro - 4H - pyrrolo - [3,2,1-i,j]-quinolin-4-one, and 3-julolidone respectively,
70 the second of these being prepared by the method of Example 34 from indoline and ethyl acetoacetate.

The known compound 1,2 - dihydro - 4H-pyrrolo - [3,2,1-i,j] - quinolin - 4 - thione
75 was similarly prepared from the corresponding 4-ketone.

Example	Structure	m.p. °C	Analysis (theoretical in brackets) C % H % N %		
40		121-3°	69.31	5.83	7.02
41		235-236.5°	71.16 (71.60)	5.37 5.52	7.47 6.97
42		73-5°	71.06 (70.93)	6.57 6.40	6.97 6.90

EXAMPLE 43.

By a similar procedure to that described in Examples 7 and 8, 9 - bromo - 2,3,6,7-tetrahydro - 1H,5H - pyrido - [3,2,1-i,j]-quinolin-3-one, m.p. 101-102°, was prepared from 3-julolidone.

Analysis:—

found:

C, 54.21; H, 4.45; N, 5.41%
calculated for C₁₂H₁₀BrNO:
C, 54.0; H, 4.51; N, 5.21%

10

EXAMPLE 44.

Phosphorus oxychloride (52g) was mixed with N-methyl formanilide (8.6g) at room temperature and then a solution of 2-lilolidone (17.2g) in ether (600 ml) was added. A homogeneous solution was formed on shaking and allowed to stand overnight, when an oily layer separated. The mixture was poured onto ice, washed with dilute acid and then with water, extracted with chloroform and the organic layer separated, dried and evaporated to yield 3.5g of crude 8-formyl-1,2,5,6-tetrahydro-4H-pyrrolo-[3,2,1-i,j]-quinolin-2-one as a yellow solid. Recrystallisation from acetic acid yielded 2.2g of product, m.p. 210—213°.

Analysis:—
found:

C, 71.63; H, 5.73; N, 7.27%
calculated for $C_{12}H_{11}NO_2$:
C, 71.7; H, 5.5; N, 6.96%

EXAMPLES 45 and 46.

The following compounds were prepared by the method of Example 34, from 1,2,3,4-tetrahydroquinoline and ethyl α -n-propyl-acetoacetate, and from 6-methoxy-1,2,3,4-tetrahydroquinoline and ethyl α -methyl-acetoacetate, respectively:

1-methyl-2-propyl-6,7-dihydro-3H,5H-pyrido-[3,2,1-i,j]-quinolin-3-one, m.p. 121—123°.

Analysis:—
found:

C, 78.97; H, 7.40; N, 6.34%
calculated for $C_{16}H_{19}NO$:

C, 79.26; H, 7.54; N, 6.16%

9-methoxy-1,2-dimethyl-6,7-dihydro-3H,5H-pyrido-[3,2,1-i,j]-quinolin-3-one, m.p. 115—117°.

Analysis:—
found:

C, 73.77; H, 7.08; N, 5.87%

calculated for $C_{14}H_{13}NO_2$:

C, 74.05; H, 7.04; N, 5.76%

EXAMPLES 47 and 48.

By a similar procedure to that described in Example 36, the following compounds were prepared from indoline and α -phenyl diethyl malonate and α -n-butyl diethyl malonate, respectively.

(a) 6-hydroxy-5-phenyl-1,2-dihydro-4H-pyrrolo-[3,2,1-i,j]-quinolin-4-one, m.p. 301—303°.

Analysis:—

found:

C, 77.47; H, 4.78; N, 5.45%

calculated for $C_{17}H_{13}NO_2$:

C, 77.55; H, 4.98; N, 5.32%

This compound is the enolic form of 5-phenyl-1,2,5,6-tetrahydro-4H-pyrrolo-[3,2,1-i,j]-quinolin-4,6-dione.

(b) 5-n-butyl-6-hydroxy-1,2-dihydro-4H-pyrrolo-[3,2,1-i,j]-quinolin-4-one, m.p. 164—166°.

Analysis:

found:

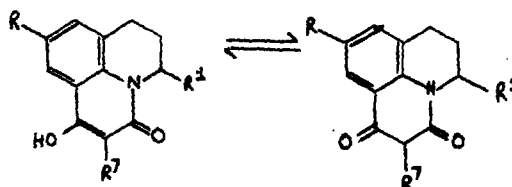
C, 73.79; H, 7.14; N, 5.60%

calculated for $C_{15}H_{17}NO_2$:

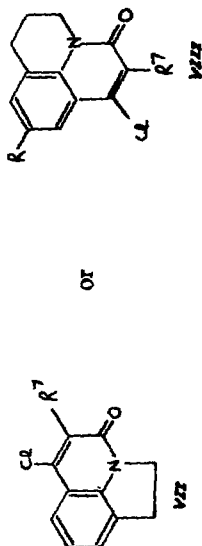
C, 74.05; H, 7.04; N, 5.76%

EXAMPLES 49 to 60.

By a similar procedure to that described in Example 36, the compounds shown in the following Table were prepared from the appropriately substituted tetrahydroquinoline and α -substituted diethyl malonate:



EXAMPLES 61 to 64.
By a similar procedure to that described in Example 38, the compounds shown in the following Table were prepared from the products of Examples 36, 51, 37 and 50, respectively:

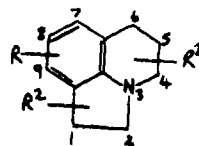


Example	Formula	R	R ⁷	m.p. °C	Analysis (calculated in brackets)		
					C	H	N
61	VII	H	CH ₃	168-170°	63.92 (63.90)	4.77 4.73	6.03 6.22)
62	VIII	CH ₃ O	H	138-9°	62.70 (62.51)	4.85 4.95	5.30 5.62)
63	VIII	H	CH ₃	121-2°	62.74 (62.76)	5.18 5.41	5.21 5.21)
64	VIII	H	C ₆ H ₅	114-6°	73.20 (73.10)	4.77 4.74	4.67 4.74)

EXAMPLE 65.

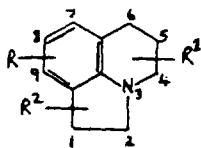
The product of Example 61 (3.3g) in ethanol (70 ml) was hydrogenated using a 5% palladium-on-carbon catalyst in a Parr hydrogenator at 60° and 60 psi until the required amount of hydrogen had been taken up. The reaction product was filtered to remove catalyst and the ethanol evaporated off to yield an off-white solid which was recrystallised from 60/80 petroleum ether to

	give 1 - methyl - 1,2,5,6 - tetrahydro - 4H-pyrrolo - [3,2,1-i,j] - quinolin - 4 - one, m.p. 81—82°.	
	Analysis:—	
5	found:	
	C, 76.84; H, 7.12; N, 7.45	
	calculated for C ₁₂ H ₁₃ NO:	
	C, 76.97; H, 7.00; N, 7.48	
10	The use of compounds of the formula I by the method according to the invention, including the novel compounds falling within the scope of the formula I, to protect rice plants against the blast disease caused by <i>Piricularia oryzae</i> is illustrated by the following Example.	
15		
	EXAMPLE 66.	
	Rice plants in the fully developed second-leaf growth stage were subjected to a spray of the test compound until run-off. Each test compound was dissolved in water, acetone, methanol or ethanol and diluted to 100 parts per million with deionised water containing a wetting agent (Span 85) and a dispersing agent (Tween 80) used at levels of 200 ppm. and 50 ppm., respectively, in the final spray. ("Span" and "Tween" are Registered Trade Marks).	
20		
25	The treated plants were allowed to dry, spray-inoculated with an aqueous spore suspension of <i>Piricularia oryzae</i> (200 spores/microscopic field at 100 X) to run-off and then placed in an incubation chamber at 70°F and 95 percent relative humidity. After about thirty hours incubation, the plants were removed to a greenhouse for disease development. Untreated plants were inoculated and treated similarly, as controls. Within five days infection lesions were sufficiently developed to permit assessment of the effectiveness of the test compounds in controlling the disease.	30
		35
	The severity of the infection was determined by actual count of the number of infection lesions appearing on the treated plants compared to the number of lesions appearing on the control plants. Phenyl mercuric acetate (PMAS) was used as a reference standard. Rice plants were treated with an aqueous spray of this standard material as described above, at a concentration of 200 ppm., at which level it was found to be 100% effective.	40
		45
	In this manner, the effectiveness of the following compounds against rice blast disease was demonstrated (at 100 parts per million unless otherwise indicated). An asterisk in the "Example" column indicates a known compound.	50
		55

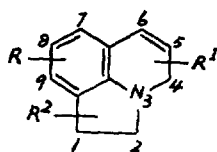


R	R ¹	R ²	Example	Effectiveness (%)
H	H	H	*(lilolidine ⁽¹⁾)	56
H	H	2-oxo	*(2-lilolidone)	100
H	4-oxo	H	*(4-lilolidone)	100
H	6-oxo	H	*(6-lilolidone)	55
H	H	1-CH ₃ -2-oxo	*	96
H	H	1-C ₆ H ₅ -2-oxo	*	37 (at 50 ppm)
8-CH ₃	H	2-oxo	1	99
8-CH ₃	H	1-C ₆ H ₅ -2-oxo	3	49
H	4-CH ₃	2-oxo	4	55
8-Cl	H	1,1-di-Cl-2-oxo	5	68
7,8-di-Cl	H	1,1-di-Cl-2-oxo	6	60
8-Br	4-oxo	H	7	98
8-Br	H	2-oxo	8	87
8-Br	H	1-Br-1-C ₆ H ₅ -2-oxo	9	53
8-Br	H	1-Br-1-CH ₃ -2-oxo	10	33
8-Br	H	1,1-di-Cl-2-oxo	11	70
8-C ₂ H ₅ CO	4-oxo	H	12	74
8-C ₂ H ₅ CO	H	1-CH ₃ -2-oxo	13	51
8-n-C ₃ H ₇ CO	H	1-CH ₃ -2-oxo	14	17
8-CH ₃ CO	H	2-oxo	15	53
8-C ₂ H ₅ CO	H	2-oxo	16	43
8-CH ₃ CO	4-oxo	H	17	92
8-C ₆ H ₅ CO	H	2-oxo	19	94
8-Cl	H	1,2-dioxo	20	38
8-Br	H	1,2-dioxo	21	56
8-Cl	H	2-oxo	22	72
8-Cl	H	1,1-di-C ₆ H ₅ -2-oxo	23	30
8-tert-C ₄ H ₉	H	2-oxo	24	99
8-HO	H	2-oxo	25	54
8-HO	H	1-CH ₃ -2-oxo	26	30
8-CH ₃ CO.O	H	1-CH ₃ -2-oxo	30	48
8-CN	H	4-oxo	31	37
H	5-CH ₃ -4,6-dioxo	H	36	53 (at 10 ppm)

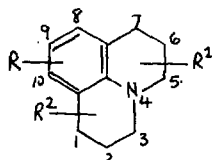
(1) as *p*-toluene sulphonate salt



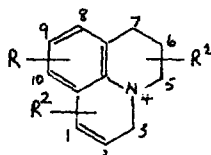
R	R ¹	R ²	Example	Effectiveness (%)
H	4-thioxo	H	39	100
H	H	2-thioxo	41	57
8-HCO	H	2-oxo	44	58
H	5CH ₃ -4-oxo	H	65	34



R	R ¹	R ²	Example	Effectiveness (%)
H	4-oxo	H	*	99
H	6-CH ₃ -4-oxo	H	*	100
H	4-thioxo	H	*	75
H	5,6-di-CH ₃ -4-oxo	H	*	40 (at 50 ppm)
H	5-C ₂ H ₅ -6-CH ₃ -4-oxo	H	34	43 (at 10 ppm)
H	6-C ₆ H ₅ -4-oxo	H	35	49
H	6-CH ₃ -4-thioxo	H	40	53 (at 10 ppm)
H	6-Cl-5-CH ₃ -4-oxo	H	61	53 (at 10 ppm)



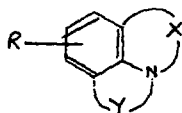
R	R ¹	R ²	Example	Effectiveness (%)
H	H	3-oxo	*(3-julolidone)	99
H	H	1,3-dioxo	*	58
9-CH ₃	H	3-oxo	2	79
9-CH ₂ CO.O	H	3-oxo	28	56
H	H	3-thioxo	42	100
H	H	2-C ₆ H ₅ -1,3-dioxo	50	64 (at 10 ppm)
H	H	2-n-C ₃ H ₇ -1,3-dioxo	53	61
H	H	2-CH ₃ -1,3-dioxo	54	63
9-CH ₃ O	H	2-C ₆ H ₅ -1,3-dioxo	55	29
9-CH ₃	H	2-iso-C ₃ H ₇ -1,3-dioxo	57	47
H	H	2-iso-C ₃ H ₇ -1,3-dioxo	58	65 (at 10 ppm)



R	R ¹	R ²	Example	Effectiveness (%)
H	H	3-oxo	*	96
H	H	1-CH ₃ -3-oxo	*	56
H	H	1-Cl-3-oxo	*	64 (at 10 ppm)
9-CH ₃	H	1-CH ₃ -3-oxo	32	31
9-CH ₃ O	H	1-CH ₃ -3-oxo	33	30
H	H	1-Cl-2-CH ₃ -3-oxo	38	52 (at 10 ppm)
9-CH ₃ O	H	1-Cl-3-oxo	62	38
H	H	1-Cl-2-CH ₃ -3-oxo	63	47
H	H	1-Cl-2-C ₆ H ₅ -3-oxo	64	39

WHAT WE CLAIM IS:—

1. A method for the treatment or control of fungal and/or bacterial diseases of plants, especially the rice plant, comprising contacting the plant, or the seeds thereof, with a fungicidally and/or bactericidally effective amount of a pyrrolo-indole, pyrrolo-quinoline or pyrido-quinoline compound of the formula:



wherein each of X and Y represents a 2- or 3-carbon chain which completes a saturated or unsaturated pyrrolo- or pyrido- ring;

the carbon chain of X and Y may each be substituted with one or more halogen atoms or lower alkyl or phenyl groups and may include one or more ketone or thioketone groups; and

R represents hydrogen or a lower alkyl, lower alkoxy, lower alkanoyl, benzoyl, hydroxy, lower alkanoyloxy or cyano group or up to two halogen atoms; or a non-phytotoxic acid addition salt thereof.

2. A method according to claim 1, in which the compound used is a compound of the formula I in which the carbon chain of either X or Y includes a single ketone or thioketone group, in a position adjacent to the ring nitrogen atom, and R is either hydrogen or a halogen, lower alkyl or lower aliphatic acyl substituent in the *para*-position to the ring nitrogen atom.

3. A method according to claim 1, in which the compound used is a compound of the formula I in which X is —CH₂CO—, —CH₂CH₂CO—, —CH=CHCO— or a corresponding thio-carbonyl group (the —CO— or —CS— group being adjacent to the ring nitrogen atom), each being optionally substituted with one or more lower alkyl or phenyl groups, Y is —CH₂CH₂— or —CH₂CH₂CH₂—, and R is hydrogen or a halogen, lower alkyl, lower alkoxy or lower alkanoyl substituent in the *para*-position to the ring nitrogen atom.

4. A method according to claim 1, in which the compound used is 2-lilolidone, 4-lilolidone, 1-methyl-2-lilolidone, 8-methyl-2-lilolidone, 8-bromo-4-lilolidone, 8-*tert*-butyl-2-lilolidone or lilolidine-4-thione.

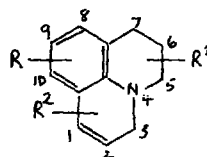
5. A method according to claim 1, in which the compound used is 1,2-dihydro-4H-pyrrolo-[3,2,1-*i,j*]-quinolin-4-one or 6-methyl-1,2-dihydro-4H-pyrrolo-[3,2,1-*i,j*]-quinolin-4-one.

6. A method according to claim 1, in which the compound used is 3-julolidone, julolidine-3-thione, or 1,2-dihydro-3H,5H-pyrido-[3,2,1-*i,j*]-quinolin-5-one.

7. A method according to any preceding claim in which the compound is added to the water in which the plant is growing.

8. A composition comprising a compound of the formula (I) together with a diluent or carrier, the composition being in the form of

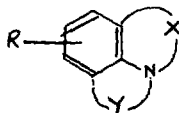
- a dust,
- a wettable powder comprising a dust as in (a) above together with a wetting agent and conditioning agent, or



R	R ¹	R ²	Example	Effectiveness (%)
H	H	3-oxo	*	96
H	H	1-CH ₃ -3-oxo	*	56
H	H	1-Cl-3-oxo	*	64 (at 10 ppm)
9-CH ₃	H	1-CH ₃ -3-oxo	32	31
9-CH ₃ O	H	1-CH ₃ -3-oxo	33	30
H	H	1-Cl-2-CH ₃ -3-oxo	38	52 (at 10 ppm)
9-CH ₃ O	H	1-Cl-3-oxo	62	38
H	H	1-Cl-2-CH ₃ -3-oxo	63	47
H	H	1-Cl-2-C ₆ H ₅ -3-oxo	64	39

WHAT WE CLAIM IS:—

1. A method for the treatment or control of fungal and/or bacterial diseases of plants, especially the rice plant, comprising contacting the plant, or the seeds thereof, with a fungicidally and/or bactericidally effective amount of a pyrrolo-indole, pyrrolo-quinoline or pyrido-quinoline compound of the formula:



wherein each of X and Y represents a 2- or 3-carbon chain which completes a saturated or unsaturated pyrrolo- or pyrido- ring;

the carbon chain of X and Y may each be substituted with one or more halogen atoms or lower alkyl or phenyl groups and may include one or more ketone or thioketone groups; and

R represents hydrogen or a lower alkyl, lower alkoxy, lower alkanoyl, benzoyl, hydroxy, lower alkanoyloxy or cyano group or up to two halogen atoms;

or a non-phytotoxic acid addition salt thereof.

2. A method according to claim 1, in which the compound used is a compound of the formula I in which the carbon chain of either X or Y includes a single ketone or thioketone group, in a position adjacent to the ring nitrogen atom, and R is either hydrogen or a halogen, lower alkyl or lower aliphatic acyl substituent in the *para*-position to the ring nitrogen atom.

3. A method according to claim 1, in which the compound used is a compound of the formula I in which X is —CH₂CO—, —CH₂CH₂CO—, —CH=CHCO— or a corresponding thio-carbonyl group (the —CO— or —CS— group being adjacent to the ring nitrogen atom), each being optionally substituted with one or more lower alkyl or phenyl groups, Y is —CH₂CH₂— or —CH₂CH₂CH₂—, and R is hydrogen or a halogen, lower alkyl, lower alkoxy or lower alkanoyl substituent in the *para*-position to the ring nitrogen atom.

4. A method according to claim 1, in which the compound used is 2-lilolidone, 4-lilolidone, 1-methyl-2-lilolidone, 8-methyl-2-lilolidone, 8-bromo-4-lilolidone, 8-*tert*-butyl-2-lilolidone or lilolidine-4-thione.

5. A method according to claim 1, in which the compound used is 1,2-dihydro-4H-pyrrolo-[3,2,1-*i,j*]-quinolin-4-one or 6-methyl-1,2-dihydro-4H-pyrrolo-[3,2,1-*i,j*]-quinolin-4-one.

6. A method according to claim 1, in which the compound used is 3-julolidone, julolidine-3-thione, or 1,2-dihydro-3H,5H-pyrrodo-[3,2,1-*i,j*]-quinolin-5-one.

7. A method according to any preceding claim in which the compound is added to the water in which the plant is growing.

8. A composition comprising a compound of the formula (I) together with a diluent or carrier, the composition being in the form of

- (a) a dust,
(b) a wettable powder comprising a dust as in (a) above together with a wetting agent and conditioning agent, or



- (c) an emulsifiable concentrate comprising the said compound and an emulsifying agent in a substantially water-immiscible organic solvent.
- 5 9. A composition as claimed in claim 8 wherein the dust contains 0.25 to 4% by weight of the active ingredient.
- 10 10. A composition as claimed in claim 8 wherein the concentrate contains from 2 to 50% by weight of the active compound.
11. A composition as claimed in any one of claims 8 to 10 wherein the compound is as defined in claim 2 or 3.
12. A composition as claimed in any one of claims 8 to 10 wherein the compound is as defined in claim 4, 5 or 6.
13. A method according to claim 1 substantially as hereinbefore described in any one of the tests of Example 66.
- 15

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Agent for the Applicants.

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